POST-EDITED MACHINE TRANSLATION

from

RISING SUN COMMUNICATIONS LTD.

(Incorporating Rotha Fullford Leopold of Canberra, Australia)

The Nightingale Centre, 8 Balham Hill, London SW12 9EA

Tel: +44 (0)20 86730865 Fax: +44 (0)20 86750009

http://www.risingsun.co.uk

PATENT No. J10-152462

Title of the Invention

Differentiation induction agent

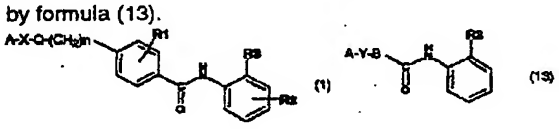
(Abstract)

(the subject)

It is to put forward novel benzamide derivative and novel anilide derivative having differentiation induction action.

(Method of Solution)

Novel benzamide derivative represented by formula (1) and novel anilide derivative represented by formula (13).



(1) (13)

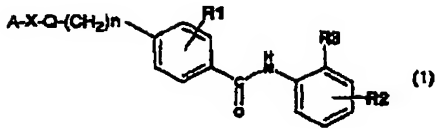
(effect)

Because novel benzamides derivative represented by formula (1) and novel anilide derivative represented by formula (13) of this invention has differentiation induction action, it is useful as therapy and/or improvement agent for malignant tumour, autoimmune disease, dermatopathia, parasite infestation. In particular it is highly effective as carcinostatic and is effective in hematopoietic organ tumour, solid cancer.

Patent Claims.

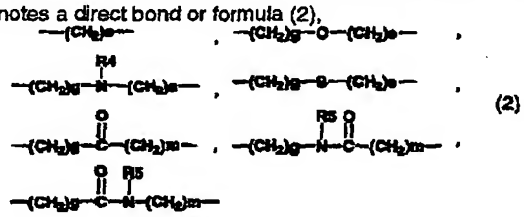
(Claim 1)

Benzamide derivatives represented by formula(1) and pharmacologically acceptable salts thereof.



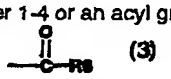
(1)

[In the formula, A denotes optionally substituted phenyl group or heterocycle (As the substituents, it has 1-4 groups selected from the group comprising halogen atom, hydroxy group, amino group, nitro group, cyano group, alkyl group of carbon number 1-4, alkoxy group of carbon number 1-4, amino alkyl group of carbon number 1-4, alkylamino group of carbon number 1-4, acyl group of carbon number 1-4, acylimino-group of carbon number 1-4, alkylthio group of carbon number 1-4, perfluoro alkyl group of carbon number 1-4, perfluoro alkyloxy group of carbon number 1-4, carboxyl group, alkoxycarbonyl group of carbon number 1-4, phenyl group or heterocycle). X denotes a direct bond or formula (2),



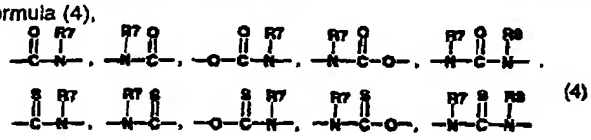
(2)

(In the formula, e denotes an integer of 1-4. The g and m respectively independently denote an integer of 0-4. R4 denotes any of the structures represented by hydrogen atom, optionally substituted alkyl group of carbon number 1-4 or an acyl group represented by formula (3),



(3)

(In the formula, R6 denotes acyl group represented by optionally substituted alkyl group of carbon number 1-4, perfluoro alkyl group of carbon number 1-4, phenyl group or heterocycle). R5 denotes hydrogen atom or optionally substituted alkyl group of carbon number 1-4), n denotes an integer of 0-4. Wherein, when X denotes a direct bond, n is not 0. Q denotes any of structures represented by formula (4),



(4)

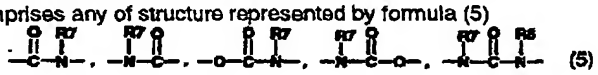
(In the formula, R7 and R8 respectively independently denote hydrogen atom or optionally substituted alkyl group of carbon number 1-4). R1 and R2 respectively independently denote hydrogen atom, halogen atom, hydroxy group, amino group, alkyl group of carbon number 1-4, alkoxy group of carbon number 1-4, amino alkyl group of carbon number 1-4, alkylamino group of carbon number 1-4, acyl group of carbon number 1-4, acylimino-group of carbon number 1-4, alkylthio group of carbon number 1-4, perfluoro alkyl group of carbon number 1-4, perfluoro alkyloxy group of carbon number 1-4, carboxyl group or alkoxycarbonyl group of carbon number 1-4. R3 denotes amino group or hydroxy group.]

(Claim 2)

Benzamide derivatives and pharmacologically acceptable salts thereof in accordance with Claim 1,wherein n is an integer of 1-4.

(Claim 3)

Benzamide derivatives and pharmacologically acceptable salts thereof in accordance with Claim 2, wherein Q comprises any of structure represented by formula (5)



(5)

(In the formula, R7 and R8 have the same said meanings.)

(Claim 4)

A benzamide derivative or a pharmacologically acceptable salt thereof in accordance with Claim 3, wherein A comprises optionally substituted heterocycle.

(Claim 5)

A benzamide derivative or a pharmacologically acceptable salt thereof in accordance with Claim 4, wherein A comprises optionally substituted pyridyl group.

(Claim 6)

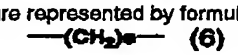
A benzamide derivatives or a pharmacologically acceptable salts in accordance with the Claim 4, wherein X comprises a direct bond.

(Claim 7)

A benzamide derivative or a pharmacologically acceptable salt thereof in accordance with Claim 6, wherein R1 and R2 comprise hydrogen atoms.

(Claim 8)
A benzamide derivative or a pharmacologically acceptable salt thereof in accordance with Claim 7, wherein R3 comprises amino group.

(Claim 9)
A benzamide derivative or a pharmacologically acceptable salt thereof in accordance with Claim 5, wherein X comprises any of structure represented by formula (6).



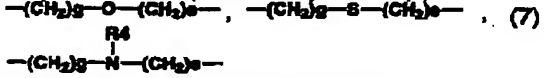
(6)

(In the formula, e has the same said meanings.)

(Claim 10)
A benzamide derivative or a pharmacologically acceptable salt thereof in accordance with Claim 9, wherein n comprises 1 and R1 and R2 comprise hydrogen atoms.

(Claim 11)
A benzamide derivative or a pharmacologically acceptable salt thereof in accordance with Claim 10, wherein R3 comprises amino group.

(Claim 12)
A benzamide derivative or a pharmacologically acceptable salt thereof in accordance with Claim 5, wherein X comprises any of structure represented by formula (7).



(7)

(In the formula, e, g and R4 have the same said meanings.)

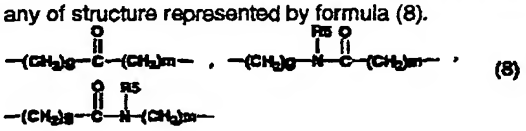
(Claim 13)
A benzamide derivative or a pharmacologically acceptable salt thereof in accordance with Claim 12, wherein n comprises 1 and R1 and R2 comprise hydrogen atoms.

(Claim 14)

A benzamide derivative or a pharmacologically acceptable salt thereof in accordance with Claim 13, wherein R3 comprises amino group.

(Claim 15)

A benzamide derivative or a pharmacologically acceptable salt thereof in accordance with Claim 5, wherein X comprises any of structure represented by formula (8).



(8)

(In the formula, g, m and R5 have the same said meanings.)

(Claim 16)

A benzamide derivative or a pharmacologically acceptable salt thereof in accordance with Claim 15, wherein n comprises 1 and R1 and R2 comprise hydrogen atoms.

(Claim 17)

A benzamide derivative or a pharmacologically acceptable salt thereof in accordance with Claim 16, wherein R3 comprises amino group.

(Claim 18)

A benzamide derivatives or a pharmacologically acceptable salts thereof in accordance with Claim 1, wherein n comprises 0.

(Claim 19)

A benzamide derivatives or a pharmacologically acceptable salts thereof in accordance with Claim 18, wherein Q comprises any of structure represented by formula (5).

(Claim 20)

A benzamide derivative or a pharmacologically acceptable salt thereof in accordance with Claim 19, wherein A comprises optionally substituted heterocycle.

(Claim 21)

A benzamide derivative or a pharmacologically acceptable salt thereof in accordance with Claim 20, wherein A comprises optionally substituted pyridyl group.

(Claim 22)

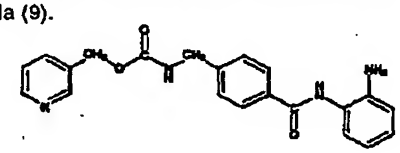
A benzamide derivative or a pharmacologically acceptable salt thereof in accordance with Claim 21, wherein R1 and R2 comprise hydrogen atoms.

(Claim 23)

A benzamide derivative or a pharmacologically acceptable salt thereof in accordance with Claim 22, wherein R3 comprises amino group.

(Claim 24)

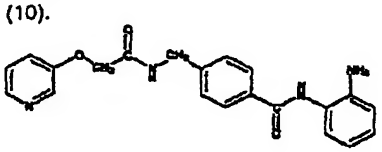
A benzamide derivatives or a pharmacologically acceptable salts thereof in accordance with Claim 1 represented by formula (9).



(9)

(Claim 25)

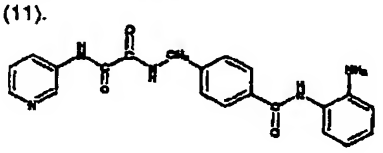
A benzamide derivatives or a pharmacologically acceptable salts thereof in accordance with Claim 1 represented by formula (10).



(10)

(Claim 26)

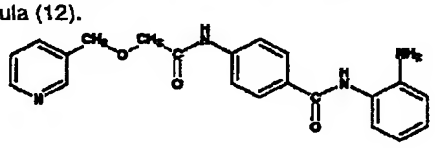
A benzamide derivatives or a pharmacologically acceptable salts thereof in accordance with Claim 1 represented by formula (11).



(11)

(Claim 27)

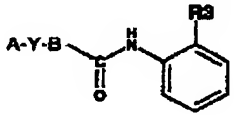
A benzamide derivatives or a pharmacologically acceptable salts thereof in accordance with Claim 1 represented by formula (12).



(12)

(Claim 28)

An anilide derivatives or a pharmacologically acceptable salts thereof represented by formula (13),



(13)

[In the formula, A denotes optionally substituted phenyl group or heterocycle (As the substituents, it has 1-4 groups selected from the group comprising halogen atom, hydroxy group, amino group, nitro group, cyano group, alkyl group of carbon number 1-4, alkoxy group of carbon number 1-4, amino alkyl group of carbon number 1-4, alkylamino group of carbon number 1-4, acyl group of carbon number 1-4, acylimino-group of carbon number 1-4, alkylthio group of carbon number 1-4, perfluoro alkyl group of carbon number 1-4, perfluoro alkyloxy group of carbon number 1-4, carboxyl group, alkoxycarbonyl group of carbon number 1-4, phenyl group or heterocycle). Y has any of -CO-, -CS-, -SO- and -SO2- in the structure and denotes a chain structure connecting A and B, cyclic structure, or a combination structure thereof. R3 denotes hydroxy group or amino group.], wherein a stereo configuration of the distance of oxygen atom or sulphur atom (W3) that forms hydrogen bond acceptor in Y and the centre of gravity (W 1) of B-ring and centre of gravity (W2) of A-ring, can conform to W1-W2 = 6.0-11.0 Å, W1-W3 = 3.0-8.0 Å, W2-W3 = 3.0-8.0 Å respectively.

(Claim 29)

An anilide derivatives or a pharmacologically acceptable salts thereof in accordance with Claim 28, wherein A comprises optionally substituted heterocycle, R3 comprises amino group, and Y comprises a chain structure connecting A to B having -CO- in the structure, cyclic structure, or a combination structure thereof.

(Claim 30)
An anilide derivatives and pharmacologically acceptable salts thereof in accordance with Claim 29, wherein B comprises optionally substituted phenyl group, W1-W2 = 7.0-9.5 Å, W1-W3 = 3.0-5.0 Å, W2-W3 = 5.0-8.0 Å.

(Claim 31)
A carcinostatic containing at least one compound in accordance with any of Claims 1-30 as effective ingredient.

(Claim 32)
A drug containing at least one compound in accordance with any of Claims 1-30 as effective ingredient.

Detailed Description of the Invention

(0001)
(Sphere of Application in Industry)
This invention is related to differentiation induction drug. More particularly it relates to the use of carcinostatic and other drugs on the basis of differentiation induction action of novel benzamide derivative or novel anilide derivative.

(0002)
(Technology of the Prior Art)
Presently among the causes of death, cancer is the highest cause exceeding cardiac disease, cerebral blood vessel, and so far many studies have been carried out with application of a large amount of cost and time. However, despite the wide ranging study for therapy methods such as surgical operation, radiotherapy, thermotherapy and the like, cancer is not yet overcome. Among these, chemotherapy is one of a large pillar of cancer therapy, but the sufficiently satisfactory drug which has not been found, and carcinostatic with high therapy effect and low toxicity is desired strongly. Many carcinostatics in the past give injury to a cancer cell by action to cells, mainly on DNA, and express cytotoxicity, and carcinostatic effect is displayed. However, because selectivity of a cancer cell from normal cell is not adequate, the side effect occurs in normal cell forms the limit of therapy.

(0003)

However, among carcinostatics, differentiation induction drug has the object of inducing differentiation of cancer cells, and suppressing the infinite proliferation of cancer cells instead of directly killing cells. Therefore it is not as effective as direct killing cell types of carcinostatic, however, but low toxicity and different selectivity are expected in retraction of cancer. Actually, it is known well the retinoic acid which is differentiation induction drug is used with therapy, and high effect is demonstrated in acute promyelocytic leukaemia (Huang et al.; Blood, 72, 567-572 (1988), Castaign et al., Blood, 76, 1704-1709 (1990), Warrell et al., New Engl. J. Med. 324, 1385-1393 (1991) and the like). Moreover because vitamin D derivative demonstrates differentiation induction action, application to carcinostatic is studied much, too (Olsson et al.; Cancer Res. 43, 5862-5867 (1983) and others).

(0004)

These study is received, and application of vitamin D derivative which is differentiation induction drug (Tokkai 6-179622), isoprene derivative (Tokkai 6-192073), tocopherol (Tokkai 6-256181), quinone derivative (Tokkai 6-305955), non cyclic poly isoprenoid (Tokkai 6-316520), benzoic acid derivative (Tokkai 7-206765), carcinostatic glycolipid (Tokkai 7-258100) have been reported. However there is not a drug which reached sufficient level for cancer curative even by these studies, and an effective drug against various cancers of high safety is desired strongly.

(0005)

Problems to be Overcome by this Invention

The object of this invention is to put forward a compound having differentiation induction action and useful as drug such as therapy • improvement drug for malignant tumour, autoimmune disease, dermatopathia, parasite infestation.

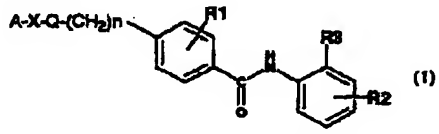
(0006)

Means to Overcome these Problems

These inventors carried out assiduous investigations to solve these problems, as a result discovered that the novel benzamide derivative and aniline derivative having differentiation induction action demonstrated antitumour effect. This invention was completed on the basis of this

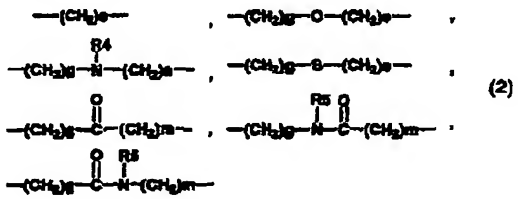
discovery. In other words this invention comprises [1] a benzamide derivative or a pharmacologically acceptable salt thereof represented by formula (1)

(0007)



[In the formula, A denotes optionally substituted phenyl group or heterocycle (containing as the substituent 1-4 groups selected from the group comprising halogen atom, hydroxy group, amino group, nitro group, cyano group, alkyl group of carbon number 1-4, alkoxy group of carbon number 1-4, amino alkyl group of carbon number 1-4, alkylamino group of carbon number 1-4, acyl group of carbon number 1-4, acylimino-group of carbon number 1-4, alkylthio group of carbon number 1-4, perfluoro alkyl group of carbon number 1-4, perfluoro alkyloxy group of carbon number 1-4, carboxyl group, alkoxycarbonyl group of carbon number 1-4, phenyl group, heterocycle), X denotes any of directly bonding or the structure represented by the formula (2)

(0008)



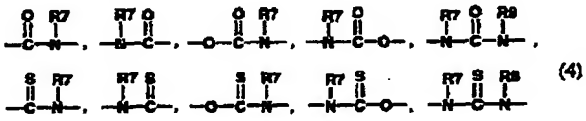
{In the formula, e denotes an integer of 1-4. The g and m respectively independently denote an integer of 0-4. R4 denotes any of the structures represented by hydrogen atom, optionally substituted alkyl group of carbon number 1-4 or an acyl group represented by formula (3),

(0009)

(In the formula, R6 denotes optionally substituted alkyl group of carbon number 1-4, perfluoro alkyl group of carbon number 1-4, phenyl group or heterocycle). R5 denotes hydrogen atom or optionally substituted alkyl group of carbon number 1-4.} n denotes an integer of 0-4. Wherein in

case of X denotes direct bond, n is not 0. Q denotes any of the structure represented by formula (4) (formula 17)

(0010)
(formula 17)



(4)

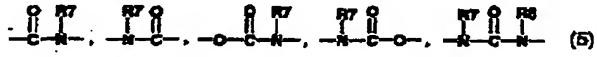
(In the formula, R7 and R8 respectively independently denote hydrogen atom or alkyl group of carbon number 1-4 that may be substituted).

(0011)
R1 and R2 respectively independently denote hydrogen atom, halogen atom, hydroxy group, amino group, alkyl group of carbon number 1-4, alkoxy group of carbon number 1-4, amino alkyl group of carbon number 1-4, alkylamino group of carbon number 1-4, acyl group of carbon number 1-4, acylimino-group of carbon number 1-4, alkylthio group of carbon number 1-4, perfluoro alkyl group of carbon number 1-4, perfluoro alkyloxy group of carbon number 1-4, carboxyl group or alkoxycarbonyl group of carbon number 1-4. R3 denotes amino group or hydroxy group], moreover,

(0012)
[2] it is benzamide derivative in accordance with [1] or pharmacologically acceptable salt, wherein n is an integer of 1-4, moreover,

(0013)
[3] it is benzamide derivative in accordance with [2] or pharmacologically acceptable salt, wherein Q is any of the structure represented by formula (5)

(0014)
(formula 18)



(5)

(in the formula, R7 and R8 have the same said meanings), moreover,

(0015)

[4] it is benzamide derivative in accordance with [3] or pharmacologically acceptable salt, wherein A is optionally substituted heterocycle, moreover,

(0016)

[5] it is benzamide derivative in accordance with [4] or pharmacologically acceptable salt, wherein A is optionally substituted pyridyl group, moreover,

(0017)

[6] it is benzamide derivative in accordance with [4] or pharmacologically acceptable salt, that X is a direct bond, moreover,

(0018)

[7] it is benzamide derivative in accordance with [6] or pharmacologically acceptable salt, wherein R1 and R2 are hydrogen atoms, moreover,

(0019)

[8] it is benzamide derivative in accordance with [7] or pharmacologically acceptable salt, wherein R3 is amino group, moreover,

(0020)

[9] it is benzamide derivative in accordance with [5] wherein X is the structure represented by formula(6) (formula 19)

(0021)

(6)

(in the formula, e has the same said meanings), or pharmacologically acceptable salt, moreover,

(0022)

[10] it is benzamide derivative in accordance with [9] or pharmacologically acceptable salt, wherein n is 1 and R1 and R2 are hydrogen atoms, moreover,

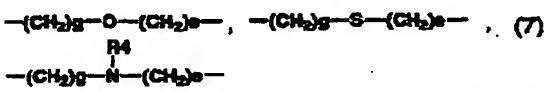
(0023)

[11] it is benzamide derivative in accordance with [10] or pharmacologically acceptable salt, wherein R3 is amino group, moreover,

(0024)

[12] it is benzamide derivative in accordance with [5] wherein X is any of the structure represented by formula(7) (formula 20),

(0025)



(in the formula, e, g and R4 have the same said meanings), or pharmacologically acceptable salt, moreover,

(0026)

[13] it is benzamide derivative in accordance with [12] or pharmacologically acceptable salt, wherein n is 1 and R1 and R2 are hydrogen atoms, moreover,

(0027)

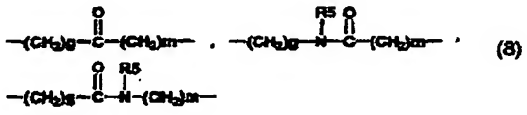
[14] it is benzamide derivative in accordance with [13] or pharmacologically acceptable salt, wherein R3 is amino group, moreover,

(0028)

[15] it is benzamide derivative in accordance with [5] wherein X is any of the structures represented by formula (8) (formula 21).

(0029)

(formula 21)



(in the formula, g, m and R5 have the same said meanings) or pharmacologically acceptable salt, moreover,

(0030)
[16] it is benzamide derivative in accordance with [15] or pharmacologically acceptable salt, wherein n is 1, and R1 and R2 are hydrogen atoms, moreover,

(0031)
[17] it is benzamide derivative in accordance with [16] or pharmacologically acceptable salt, wherein R3 is amino group, moreover,

(0032)
[18] it is benzamide derivative in accordance with [1] or pharmacologically acceptable salt, wherein n is 0, moreover,

(0033)
[19] it is benzamide derivative in accordance with [18] or pharmacologically acceptable salt, wherein Q is any of structure represented by formula (5), moreover,

(0034)
[20] it is benzamide derivative in accordance with [19] or pharmacologically acceptable salt, wherein A is optionally substituted heterocycle, moreover,

(0035)
[21] it is benzamide derivative in accordance with [20] or pharmacologically acceptable salt, wherein A is optionally substituted pyridyl group, moreover,

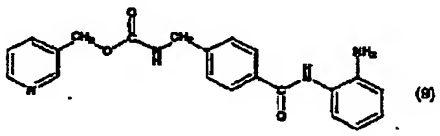
(0036)
[22] it is benzamide derivative in accordance with [21] or pharmacologically acceptable salt, wherein R1 and R2 are hydrogen atoms, moreover,

(0037)

[23] it is benzamide derivative in accordance with [22] or pharmacologically acceptable salt, wherein R3 is amino group, moreover,

(0038)
[24] it is benzamide derivative in accordance with [1] which is represented by formula (9) (formula 22).

(0039)
(formula 22)

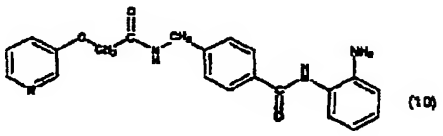


(9)

or pharmacologically acceptable salt, moreover,

(0040)
[25] it is benzamide derivative in accordance with [1] which is represented by formula (10) (formula 23).

(0041)
(formula 23)

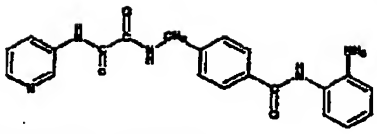


(10)

or pharmacologically acceptable salt, moreover,

(0042)
[26] it is benzamide derivative in accordance with [1] which is represented by formula (11) (formula 24).

(0043)
(formula 24)



(11)

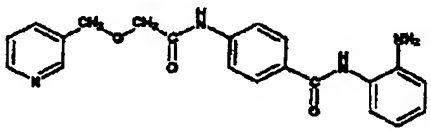
or pharmacologically acceptable salt, moreover,

(0044)

[27] it is benzamide derivative in accordance with [1] which is represented by formula (12) (formula 25).

(0045)

(formula 25)



(12)

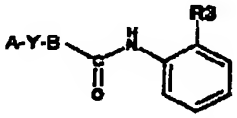
or pharmacologically acceptable salt, moreover,

(0046)

[28] it is benzamide derivative of the kind wherein it is represented by formula (13) (formula 26).

(0047)

(formula 26)



(13)

[In the formula, A denotes optionally substituted phenyl group or heterocycle (As the substituents, it has 1-4 groups selected from the group comprising halogen atom, hydroxy group, amino group, nitro group, cyano group, alkyl group of carbon number 1-4, alkoxy group of carbon number 1-4, amino alkyl group of carbon number 1-4, alkylamino group of carbon number 1-4, acyl group of carbon number 1-4, acylimino-group of carbon number 1-4, alkylthio group of carbon number 1-4, perfluoro alkyl group of carbon number 1-4, perfluoro alkyloxy group of

carbon number 1-4, carboxyl group, alkoxycarbonyl group of carbon number 1-4, phenyl group or heterocycle).

(0048)
Y has any of -CO-, -CS-, -SO- and -SO2- in the structure and denotes a chain structure connecting A and B, cyclic structure, or a combination structure thereof. R3 denotes hydroxy group or amino group.], wherein a stereo configuration of the distance of oxygen atom or sulphur atom (W3) that forms hydrogen bond acceptor in Y and the centre of gravity (W1) of B-ring and centre of gravity (W2) of A-ring, can conform to W1-W2 = 6.0-11.0 Å, W1-W3 = 3.0-8.0 Å, W2-W3 = 3.0-8.0 Å respectively, or pharmacologically acceptable salt, moreover,

(0049)
[29] it is benzamide derivative in accordance with [28] or pharmacologically acceptable salt, wherein A comprises optionally substituted heterocycle, R3 comprises amino group, and Y comprises a chain structure connecting A to B having -CO- in the structure, cyclic structure, or a combination structure thereof, moreover,

(0050)
[30] it is benzamide derivative in accordance with [29] or pharmacologically acceptable salt, wherein B comprises optionally substituted phenyl group, W1-W2 = 7.0-9.5 Å, W1-W3 = 3.0-5.0 Å, W2-W3 = 5.0-8.0 Å, moreover,

(0051)
[31] it is a carcinostatic containing at least one compounds in accordance with any of [1]-[30] as effective ingredient, moreover,

(0052)
[32] it is a drug containing at least one compounds in accordance with any of [1]-[30] as effective ingredient.

(0053)
Conditions for carrying out this invention

Below, this invention is described in greater detail. As carbon number 1-4 stated in this invention, the carbon number per the unit substituent is denoted. In other words, in case of for example dialkyl substitution the carbon number 2-8 is denoted.

(0054)
The heterocycle in the compound represented by formula (1) comprises monocyclic heterocycle or bicyclic condensed heterocycle comprising 5 membered ring or 6 membered ring containing 1-4 sulphur atom, oxygen atom or nitrogen atom, and as monocyclic heterocycle, for example pyridine, pyrazine, pyrimidine, pyridazine, thiophene, furan, pyrrole, pyrazole, isooxazole, isothiazole, imidazole, oxazole, thiazole, piperidine, piperazine, pyrrolidine, quinacridine, tetrahydrofuran, morpholine, thiomorpholine and the like are nominated and as bicyclic condensed heterocycle, for example condensed pyridine ring such as quinoline, isoquinoline, naphthyridine, furopyridine, thienopyridine, pyrrolopyridine, oxazolo pyridine, imidazolo pyridine, thiazolopyridine and the like, benzofuran, benzo thiophene, benzimidazole and the like are nominated.

(0055)
As halogen atom, fluorine atom, chlorine atom, bromine atom and iodine atom are nominated. As alkyl group of carbon number 1-4, for example methyl group, ethyl group, n-propyl group, isopropyl group, n-butyl group, isobutyl group, sec-butyl group, t-butyl group are nominated.

(0056)
As alkoxy group of carbon number 1-4, for example methoxy group, ethoxy group, n-propoxy group, isopropoxy group, allyloxy group, n-butoxy group, isobutoxy group, sec-butoxy group, t-butoxy group are nominated. As amino alkyl group of carbon number 1-4, for example aminomethyl group, 1-amino ethyl group, 2-aminopropyl group are nominated.

(0057)
As alkylamino group of carbon number 1-4, for example N-methylamino group, N,N-dimethylamino group, N,N-diethylamino group, N-methyl-N-ethylamino group, N,N-diisopropylamino group are nominated. As acyl group of carbon number 1-4, for example acetyl group, propanoyl group, butanoyl group are nominated.

(0058)

As acylamino-group of carbon number 1-4, for example acetylamino group, propanoyl amino group, butanoyl amino groups are nominated. As alkylthio group of carbon number 1-4, methylthio group, ethylthio group, propylthio group are nominated.

(0059)

As perfluoro alkyl group of carbon number 1-4, for example trifluoromethyl group, pentafluoro ethyl groups are nominated. As perfluoro alkyloxy group of carbon number 1-4, for example trifluoro methoxy group, pentafluoro ethoxy group are nominated.

(0060)

As alkoxycarbonyl group of carbon number 1-4, for example methoxycarbonyl group, ethoxycarbonyl group are nominated. As alkyl group of carbon number 1-4 that may be substituted, for example, methyl group, ethyl group, n-propyl group, isopropyl group, n-butyl group, isobutyl group, sec-butyl group, t-butyl group and the like, and the one having as the substituent thereof 1-4 groups selected from the group comprising halogen atom, hydroxy group, amino group, nitro group, cyano group, phenyl group, heterocycle.

(0061)

The important factors for demonstrating the high differentiation induction activity in the compound represented formula (13), are [a] presence of ring A, ring B and oxygen atom or sulphur atom as hydrogen bond acceceptor and [b] the distances specified by their steric configuration as described hereinafter. Accordingly Y is not restricted in particular if it is structure that has hydrogen bond receptor in structure thereof, and prescribes steric configuration of ring A and ring B to the necessary locations. In other words, the structure of Y having any of -CO-, -CS-, -SO- or -SO2- in the structure, and comprising chain form connecting A and B or cyclic or a combination thereof means either of [a] a linear or branched chain form structure comprising carbon atom or heteroatom, which contains a structure containing -CO-, -CS-, -SO-, -SO2- in the structure that connects A and B, [b] a structure that connects A and B having -CO-, -CS-, -SO-, -SO2- in the cyclic structure, or [c] a structure in which cyclic structure and chain form structure are combined which contains -CO-, -CS-, -SO-, -SO2- connecting A and B in the structure.

(0062)

As basic structure of cyclic structure, ring structure containing carbon atom of 4-7 membered ring or heteroatom or condensed ring of these is nominated. Cyclobutane ring, cyclopetane ring, cyclohexane ring, cyclo heptane, oxetane ring, oxolane ring, oxane ring, oxepan ring, pyrrolidine ring, imidazo lysine ring, pyrazolidine ring, piperidine ring, piperazine ring, indoline ring, thiolane ring, thiazolidine ring, oxazolidinyl ring are proposed, and unsaturated bond, hydrogen bond receptor and the substituent can be present in the structure thereof.

(0063)
By carrying out analysis considering the degree of freedom of conformation of the compound represented by formula (13), it was discovered that atomic group considered to be involved in living body-drug interaction such as hydrophobic interaction and hydrogen bond assumed specific spatial arrangement in the compounds which demonstrated high differentiation induction activity.

(0064)
In an embodiment, three dimensional structures of highly active compounds were generated using molecule modelling software (SYBYL6.3), and the most stable structure was determined by carrying out conformational analysis with respect to all rotatable bonds. Wherein as for the evaluation of energy, charge was generated on each atom by Gasteiger-Huckel method, and next it was performed using Tripos force field. Thereafter, using the most stable structure as the starting structure, overlapping which considered conformation was performed by DISCO/SYBYL. As a result one specific spatial arrangement was found to be required to express high differentiation induction activity.

(0065)
In aforesaid analysis procedure, analysis can be performed by using other commercial calculation package [CATALYST (MSI company), Cerius2/QSAR+ (MSI Company), SYBYL/DISCO (Tripos Company)], and the distance information obtained in this invention, and is not restricted by specific calculation program.

(0066)
Centre of gravity of ring used in the definition of spatial arrangement can be defined as average of X, Y and Z axis of atom composing the ring. Moreover, when the subject ring structure is a

condensed multiple ring system, either the centre of gravity of the whole condensed ring or the centre of gravity of ring of part thereof can be used as centre of gravity to define space.

(0067)
To be able to assume stereo configuration means that the conformers that satisfy the stereo configuration are present within 15 kcal/mol from the most stable structure in terms of energy, but, preferably, it is present within 8 kcal/mol during. The details of calculation technique can be carried out according to Sybyl manual: M.Clark or J. Comput. Chem. 10. 982 (1989).

(0068)
As salt of the pharmacologically acceptable compound, inorganic acid such as hydrochloric acid, hydrobromic acid, sulphuric acid, orthophosphoric acid used regularly in this sphere and salt of organic acid such as acetic acid, lactic acid, tartaric acid, malic acid, succinic acid, fumaric acid, maleic acid, citric acid, benzoic acid, trifluoroacetic acid, p-toluenesulfonic acid, methanesulfonic acid are nominated. For example N-(2-aminophenyl)-4-(N-(pyridin-3-yl) methoxycarbonylamino methyl) benzamide hydrochloride, N-(2-aminophenyl)-4-(N-(pyridin-3-yl) methoxycarbonylamino methyl) benzamide hydrobromic acid salt, N-(2-aminophenyl)-4-(N-(pyridin-3-yl) methoxycarbonylamino methyl) benzamide sulphate,

(0069)
N-(2-aminophenyl)-4-(N-(pyridin-3-yl) methoxycarbonylamino methyl) benzamide phosphate, N-(2-aminophenyl)-4-(N-(pyridin-3-yl) methoxycarbonylamino methyl) benzamide acetic acid salt, N-(2-aminophenyl)-4-(N-(pyridin-3-yl) methoxycarbonylamino methyl) benzamide lactate, N-(2-aminophenyl)-4-(N-(pyridin-3-yl) methoxycarbonylamino methyl) benzamide tartaric acid, N-(2-aminophenyl)-4-(N-(pyridin-3-yl) methoxycarbonylamino methyl) benzamide malate, N-(2-aminophenyl)-4-(N-(pyridin-3-yl) methoxycarbonylamino methyl) benzamide succinate, N-(2-aminophenyl)-4-(N-(pyridin-3-yl) methoxycarbonylamino methyl) benzamide fumarate,

(0070)
N-(2-aminophenyl)-4-(N-(pyridin-3-yl) methoxycarbonylamino methyl) benzamide maleate, N-(2-aminophenyl)-4-(N-(pyridin-3-yl) methoxycarbonylamino methyl) benzamide citrate, N-(2-aminophenyl)-4-(N-(pyridin-3-yl) methoxycarbonylamino methyl) benzamide trifluoroacetic acid, N-(2-aminophenyl)-4-(N-(pyridin-3-yl) methoxycarbonylamino methyl) benzamide p-

toluenesulfonate, N-(2-aminophenyl)-4-(N-(pyridin-3-yl) methoxycarbonylamino methyl) benzamide methanesulfonate are nominated.

(0071)

The drug denotes therapy and/or improvement drug for autoimmune disease, dermatopathia, parasite infestation in addition to carcinostatic.

(0072)

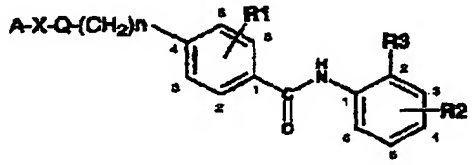
When the compound represented by formula (1) and formula (13) contains asymmetric carbon, it can be present in a form of mixture of stereoisomerism form including different stereoisomerism forms or the racemic form. In other words this invention includes various kinds of forms prescribed like these, but these can be used as the effective ingredient compound in the same way.

(0073)

Hereinafter the typical compounds represented by formula (1) of this invention and formula (13) are exemplified using embodiments in table-1 (table 1-table 24), table-2 (table 25-table 26), table-3 (table 27-table 28) and table-4 (table 29-table 30). Moreover this invention is not restricted to these examples.

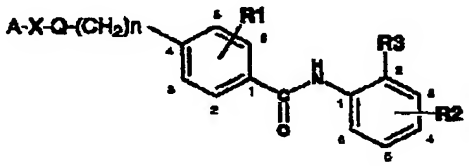
(0074)

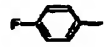
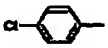
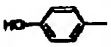
(Table 1) .



化合物番号	A	X	Q	n	R1	R2	R3
1		直接結合		1	H	H	NH_2
2		$-CH_2-$		0	H	H	NH_2
3		$-(CH_2)_2-$		0	H	H	NH_2
4		$-(CH_2)_3-$		0	H	H	NH_2
5		$-(CH_2)_4-$		0	H	H	NH_2
6		$-CH_2-$		1	H	H	NH_2
7		$-(CH_2)_2-$		1	H	H	NH_2
8		$-CH_2-$		0	H	H	NH_2
9		$-(CH_2)_2-$		0	H	H	NH_2
10		直接結合		1	H	H	NH_2

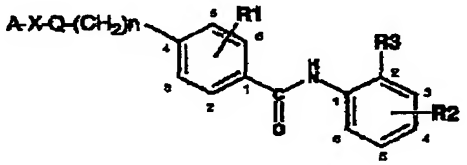
【0075】　　【表2】表－1続きの1

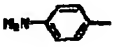
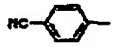
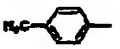
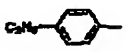
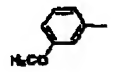


化合物番号	A	X	Q	n	R1	R2	R3
11		$-CH_2-$		1	H	H	NH_2
12		直接結合		1	H	H	NH_2
13		直接結合		1	H	H	NH_2
14		直接結合		1	H	H	NH_2
15		$-CH_2-$		0	H	H	NH_2
16		直接結合		1	H	H	NH_2
17		直接結合		1	H	H	NH_2
18		直接結合		1	H	H	NH_2
19		$-CH_2-$		0	H	H	NH_2
20		直接結合		1	H	H	NH_2

【0076】

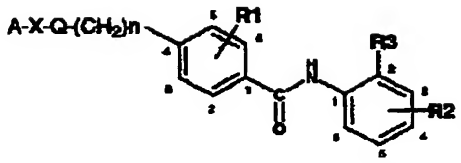
【表3】表－1続きの2



化合物番号	A	X	Q	n	R1	R2	R3
21		$-CH_2-$		0	H	H	NH_2
22		$-CH_2-$		0	H	H	NH_2
23		$-CH_2-$		1	H	H	NH_2
24		直接結合		1	H	H	NH_2
25		直接結合		1	H	H	NH_2
26		$-CH_2-$		0	H	H	NH_2
27		直接結合		1	H	H	NH_2
28		直接結合		1	H	H	NH_2
29		直接結合		1	H	H	NH_2
30		直接結合		1	H	H	NH_2

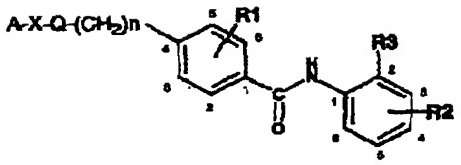
【0077】

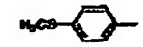
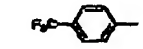
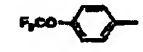
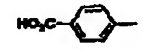
【表4】表－1続きの3



化合物番号	A	X	Q	n	R1	R2	R3
31	H_3CO-	直接結合	-C(=O)-NH-	1	H	H	NH_2
32	H_3CO-	$-CH_2-$	-C(=O)-NH-	0	H	H	NH_2
33	H_3CO, H_3CO, H_3CO-	直接結合	-C(=O)-NH-	1	H	H	NH_2
34	H_3CO, H_3CO, H_3CO-	$-CH_2-$	-O-C(=O)-NH-	1	H	H	NH_2
35	H_3CHN-	直接結合	-C(=O)-NH-	1	H	H	NH_2
36	$(H_3C)_2N$-	直接結合	-C(=O)-NH-	1	H	H	NH_2
37	H_2N-	直接結合	-NH-C(=O)-NH-	1	H	H	NH_2
38	H_3CHN-C(=O)-	$-CH_2-$	-O-C(=O)-NH-	1	H	H	NH_2
39	H_3C-C(=O)-NH-	$-CH_2-$	-O-C(=O)-NH-	1	H	H	NH_2
40	H_3C-C(=O)-	直接結合	-C(=O)-NH-	1	H	H	NH_2

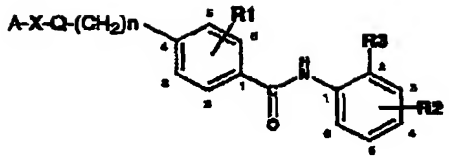
【0078】　　【表5】表－1続きの4

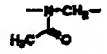
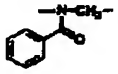


化合物番号	A	X	Q	n	R1	R2	R3
41		直接結合		1	H	H	NH_2
42		直接結合		1	H	H	NH_2
43		$-CH_2-$		0	H	H	NH_2
44		直接結合		1	H	H	NH_2
45		直接結合		1	H	H	NH_2
46		直接結合		1	H	H	NH_2
47		$-CH_2-$		1	H	H	NH_2
48		$-O-CH_2-$		1	H	H	NH_2
49		$-S-CH_2-$		1	H	H	NH_2
50		$-\underset{H}{N}-CH_2-$		1	H	H	NH_2

【0079】

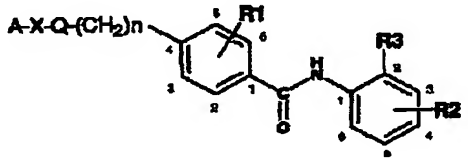
【表6】表－1続きの5



化合物番号	A	X	Q	n	R1	R2	R3
51		$-CH_2-$		1	H	H	NH_2
52		$-CH_2-$		1	H	H	NH_2
53		$-CH_2-$		0	H	H	NH_2
54		$-O-CH_2-$		0	H	H	NH_2
55		$-O-CH_2-$		0	H	H	NH_2
56		$-O-CH_2-$		1	H	H	NH_2
57		$-O-CH_2-$		1	H	5-F	NH_2
58		$-CH_2-O-CH_2-$		0	H	H	NH_2
59				1	H	H	NH_2
60				1	H	H	NH_2

【0080】

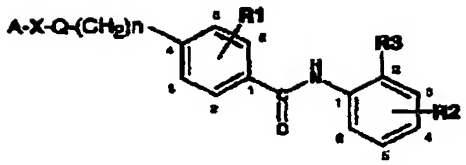
【表7】表－1続きの6



化合物番号	A	X	Q	n	R1	R2	R3
61		-O-CH2-		1	H	H	NH2
62		-O-(CH2)2-		1	H	H	NH2
63		-NH-CH2-		1	H	H	NH2
64		-S-CH2-		1	H	H	NH2
65		-O-CH2-		0	H	H	NH2
66		-O-(CH2)2-		0	H	H	NH2
67		-O-(CH2)3-		0	H	H	NH2
68		-CH2-		0	H	H	NH2
69		-(CH2)2-		0	H	H	NH2
70		-(CH2)3-		0	H	H	NH2

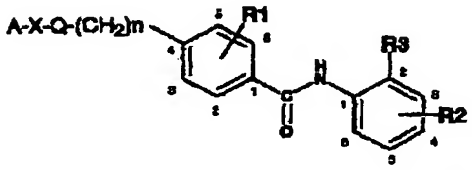
【0081】

【表8】表－1続きの7



化合物番号	A	X	Q	n	R1	R2	R3
71		直接結合		1	H	H	NH_2
72		直接結合		2	H	H	NH_2
73		直接結合		3	H	H	NH_2
74		$-CH_2-$		1	H	H	NH_2
75		$-(CH_2)_2-$		1	H	H	NH_2
76		$-(CH_2)_3-$		1	H	H	NH_2
77		$-CH_2-$		2	H	H	NH_2
78		$-CH_2-$		1	H	H	NH_2
79		直接結合		2	H	H	NH_2
80		$-CH_2-$		2	H	H	NH_2

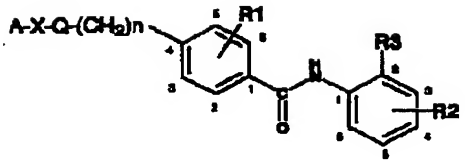
【0082】　　【表9】表－1続きの8

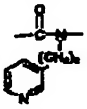
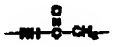
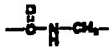
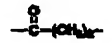
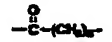


化合物番号	A	X	Q	n	R1	R2	R3
81		直接結合		1	H	H	NH_2
82		$-CH_2-$		1	H	H	NH_2
83		$-(CH_2)_2-$		1	H	H	NH_2
84		$-(CH_2)_3-$		1	H	H	NH_2
85		$-CH_2-$		1	H	H	NH_2
86		$-CH_2-$		1	H	H	NH_2
87		直接結合		1	H	H	NH_2
88		$-CH_2-$		1	H	H	NH_2
89		$-(CH_2)_2-$		1	H	H	NH_2
90		$-CH_2-$		1	H	H	NH_2

【0083】

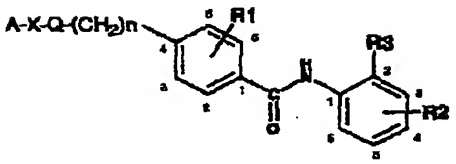
【表10】表－1続きの9

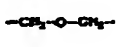
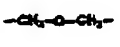
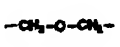
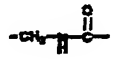
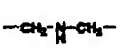
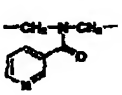
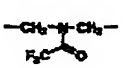
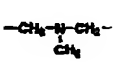
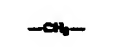
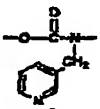
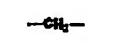


化合物番号	A	X	Q	n	R1	R2	R3
91				1	H	H	NH_2
92				1	H	H	NH_2
93				1	H	H	OH
94				0	H	H	NH_2
95				1	H	H	NH_2
96				1	H	H	NH_2
97				0	H	H	NH_2
98				1	H	H	NH_2
99				0	H	H	NH_2
100				1	H	H	NH_2

【0084】

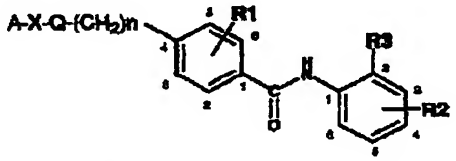
【表11】表－1続きの10

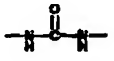
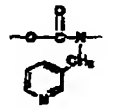
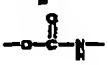
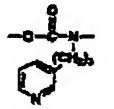


化合物番号	A	X	Q	n	R1	R2	R3
101				0	H	H	NH_2
102				0	3-CH_3	H	NH_2
103				0	H	H	NH_2
104				0	H	H	NH_2
105				0	H	H	NH_2
106				0	H	H	NH_2
107				1	H	H	NH_2
108				0	H	H	NH_2
109				1	H	H	NH_2
110				1	H	5-F	NH_2

【0085】

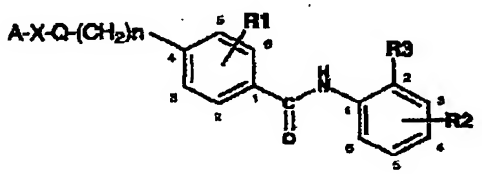
【表12】表－1続きの11

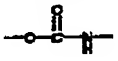
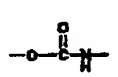


化合物番号	A	X	Q	n	R1	R2	R3
111				1	H	H	OH
112				1	H	5-F	NH_2
113				1	H	4-Cl	NH_2
114				1	H	H	OH
115				1	H	H	OH
116				1	H	4-OH	OH
117				1	H	H	OH
118				1	H	5-CH_3	OH
119				1	H	6-OCH_3	OH
120				1	H	H	NH_2

【0086】

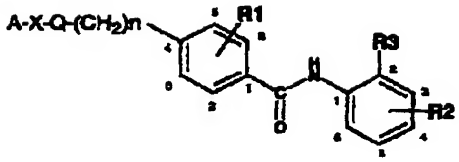
【表13】表－1続きの12

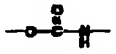
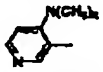
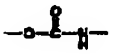
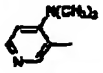
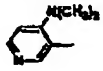
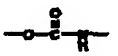
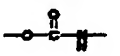


化合物番号	A	X	Q	n	R1	R2	R3
121		$-CH_2-$		1	H	5-OCH_3	NH_2
122		$-(CH_2)_3-$		0	H	5-F	NH_2
123		$-(CH_2)_2-$		0	3-Cl	H	NH_2
124		$-(CH_2)_2-$		0	H	H	NH_2
125		$-(CH_2)_2-$		1	H	H	OH
126				1	H	H	NH_2
127				1	H	H	NH_2
128		$-O-CH_2-$		1	2-Cl	H	NH_2
129		$-O-CH_2-$		1	H	5-F	NH_2
130		$-O-CH_2-$		1	H	5-OCH_3	NH_2

〔0087〕

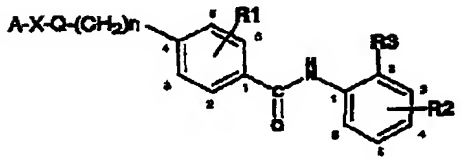
〔表14〕表－1続きの13

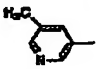
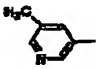
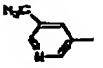


化合物番号	A	X	Q	n	R1	R2	R3
131		$-CH_2-$		1	H	H	NH_2
132		$-O-CH_2-$		1	H	H	NH_2
133		$-CH_2-O-CH_2-$		1	H	H	NH_2
134		$-CH_2-$		1	H	H	NH_2
135		$-O-CH_2-$		1	H	H	NH_2
136		$-CH_2-O-CH_2-$		1	H	H	NH_2
137		$-CH_2-$		1	H	H	NH_2
138		$-O-CH_2-$		1	H	H	NH_2
139		$-CH_2-O-CH_2-$		1	H	H	NH_2
140		$-CH_2-$		1	H	5-F	NH_2

【0088】

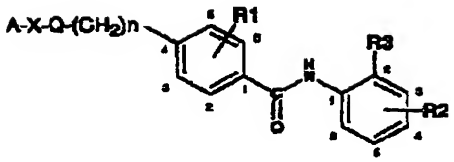
【表15】表－1続きの14

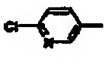


化合物番号	A	X	Q	n	R1	R2	R3
141		直接結合		1	H	H	NH_2
142		$-CH_2-$		1	H	H	NH_2
143		直接結合		1	H	H	NH_2
144		$-CH_2-$		1	H	H	NH_2
145		$-CH_2-$		1	H	H	NH_2
146		$-CH_2-$		1	H	H	NH_2
147		$-CH_2-$		1	H	H	NH_2
148		$-CH_2-$		1	H	H	NH_2
149		$-CH_2-$		1	H	H	NH_2
150		$-(CH_2)_2-$		1	H	H	NH_2

【0089】

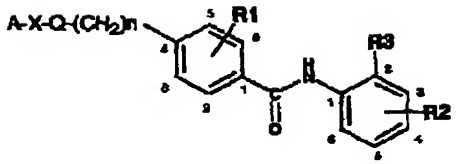
【表16】表－1続きの15

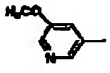
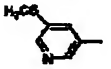
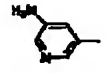


化合物番号	A	X	Q	n	R1	R2	R3
151				1	H	H	NH_2
152				0	H	H	NH_2
153				2	H	H	NH_2
154		直接結合		1	H	H	NH_2
155				1	H	H	NH_2
156		直接結合		1	H	H	NH_2
157				1	H	H	NH_2
158				1	H	H	NH_2
159				1	H	H	NH_2
160				1	H	H	NH_2

【0090】

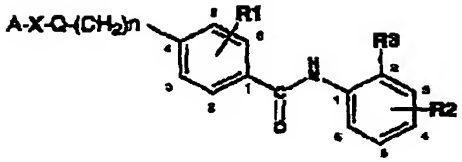
【表17】表－1続きの16



化合物番号	A	X	Q	n	R1	R2	R3
161				1	H	H	
162				1	H	H	
163				1	H	H	
164				1	H	H	
165				1	H	H	
166				0	H	H	
167				2	H	H	
168				1	H	H	
169				1	H	H	
170				1	H	H	

【0091】

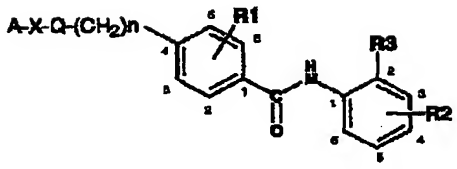
【表18】表－1続きの17



化合物番号	A	X	Q	n	R1	R2	R3
171		$-CH_2-$		1	H	H	NH_2
172		$-(CH_2)_2-$		1	H	H	NH_2
173		直接結合		1	H	H	NH_2
174		$-CH_2-$		0	H	H	NH_2
175		$-O-CH_2-$		1	H	5-OCH_3	NH_2
176		$-CH_2-O-CH_2-$		0	H	H	NH_2
177		$-CH_2-$		0	H	H	NH_2
178		直接結合		1	H	H	NH_2
179		$-CH_2-$		1	H	H	NH_2
180		$-CH_2-$		1	H	H	NH_2

【0092】

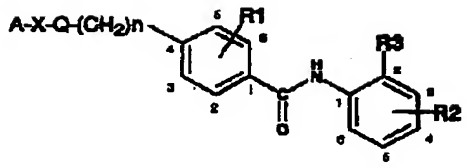
【表19】表－1続きの18



化合物番号	A	X	Q	n	R1	R2	R3
181		$-CH_2-$		1	H	H	NH_2
182		$-(CH_2)_2-$		1	H	H	NH_2
183		直接結合		1	H	H	NH_2
184		$-CH_2-$		0	H	H	NH_2
185		$-CH_2-$		0	H	H	NH_2
186		$-CH_2-$		1	H	H	NH_2
187		$-CH_2-$		0	H	H	NH_2
188		直接結合		1	H	H	NH_2
189		$-CH_2-$		1	H	H	NH_2
190		$-CH_2-$		1	H	H	NH_2

【0093】

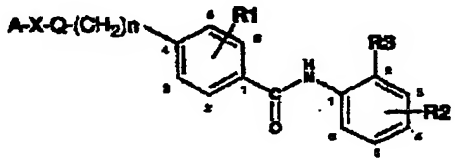
【表20】表－1続きの19



化合物番号	A	X	Q	n	R1	R2	R3
191		直接結合		1	H	H	NH_2
192		$-CH_2-$		1	H	H	NH_2
193		$-CH_2-O-CH_2-$		1	H	H	NH_2
194		$-CH_2-O-CH_2-$		0	H	H	NH_2
195		直接結合		1	H	H	NH_2
196		$-CH_2-$		1	H	H	NH_2
197		直接結合		1	H	H	NH_2
198		$-CH_2-$		1	H	H	NH_2
199		$-CH_2-O-CH_2-$		1	H	H	NH_2
200		$-CH_2-O-CH_2-$		0	H	H	NH_2

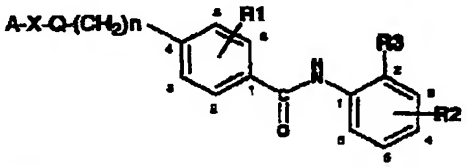
【0094】

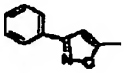
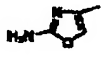
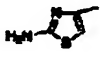
【表21】表−1続きの20



化合物番号	A	X	Q	n	R1	R2	R3
201		直接結合		1	H	H	NH_2
202		$-CH_2-$		1	H	H	NH_2
203		$-(CH_2)_2-$		1	H	H	NH_2
204		$-CH_2-O-CH_2-$		0	H	H	NH_2
205		直接結合		1	H	H	NH_2
206		$-CH_2-$		1	H	H	NH_2
207		$-CH_2-O-CH_2-$		1	H	H	NH_2
208		$-CH_2-O-CH_2-$		0	H	H	NH_2
209		直接結合		1	H	H	NH_2
210		直接結合		1	H	H	NH_2

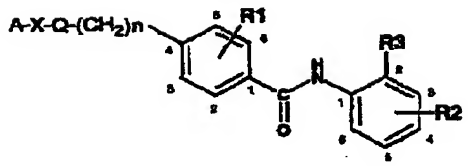
【0095】　　【表22】表－1続きの21



化合物番号	A	X	Q	n	R1	R2	R3
211				1	H	H	NH_2
212		直接結合		1	H	H	NH_2
213		直接結合		1	H	H	NH_2
214		直接結合		1	H	H	NH_2
215				1	H	H	NH_2
216				1	H	H	NH_2
217				1	H	H	NH_2
218				1	H	H	NH_2
219				1	H	H	NH_2
220				1	H	H	NH_2

【0096】

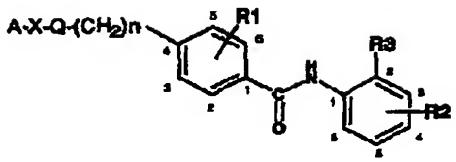
【表23】表－1続きの22

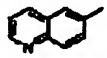
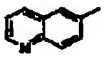
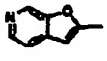
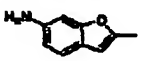
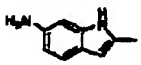


化合物番号	A	X	Q	n	R1	R2	R3
221		$-CH_2-$		1	H	H	NH_2
222		$-CH_2-O-CH_2-$		1	H	H	NH_2
223		$-CH_2-O-CH_2-$		1	H	H	NH_2
224		直接結合		1	H	H	NH_2
225		$-CH_2-$		1	H	H	NH_2
226		$-CH_2-O-CH_2-$		1	H	H	NH_2
227		$-(CH_2)_2-$		1	H	H	NH_2
228		直接結合		1	H	H	NH_2
229		$-CH_2-$		1	H	H	NH_2
230		$-CH_2-O-CH_2-$		1	H	H	NH_2

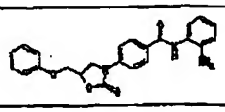
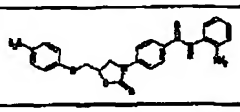
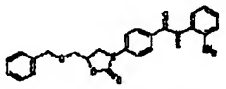
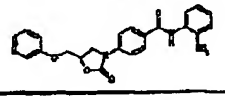
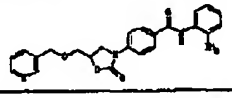
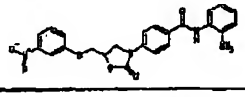
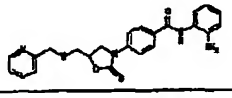
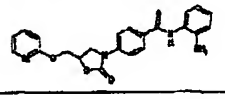
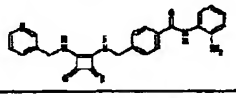
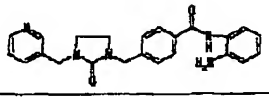
【0097】

【表24】表−1続きの23



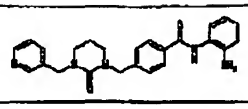
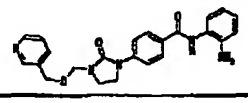
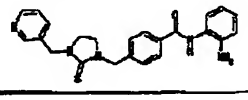
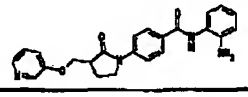
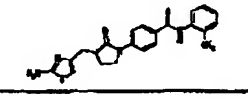
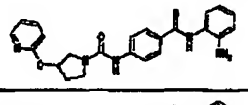
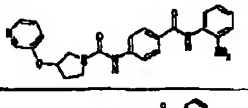
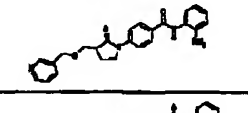
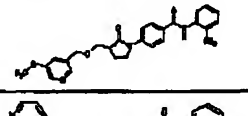
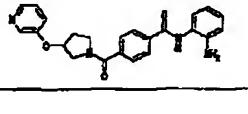
化合物番号	A	X	Q	n	R1	R2	R3
231		直接結合		1	H	H	NH_2
232		直接結合		1	H	H	NH_2
233		直接結合		1	H	H	NH_2
234		直接結合		1	H	H	NH_2
235		直接結合		1	H	H	NH_2
236		直接結合		1	H	H	NH_2
237		直接結合		1	H	H	NH_2
238		直接結合		1	H	H	NH_2
239		直接結合		1	H	H	NH_2
240		直接結合		1	H	H	NH_2

【0098】　　【表25】表－2

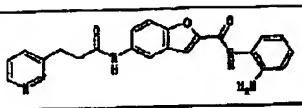
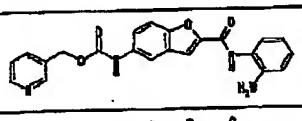
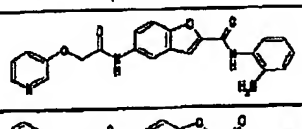
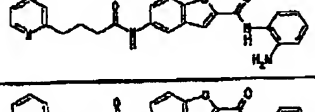
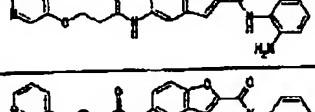
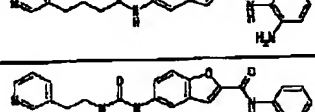
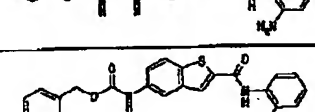
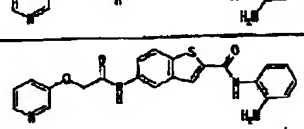
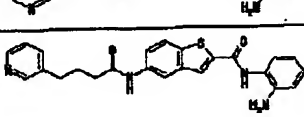
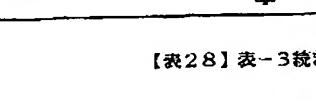
1	
2	
3	
4	
5	
6	
7	
8	
9	
10	

【0099】

【表26】表－2続きの1

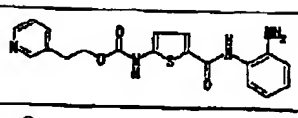
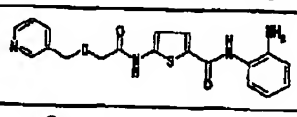
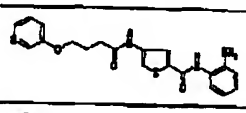
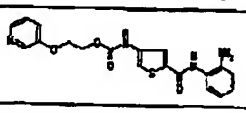
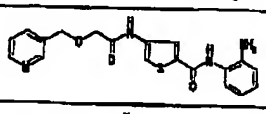
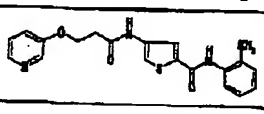
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	

【0100】　　【表27】表−3

1	
2	
3	
4	
5	
6	
7	
8	
9	
10	

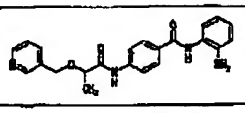
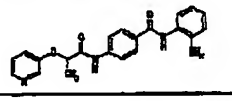
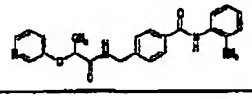
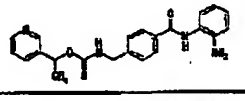
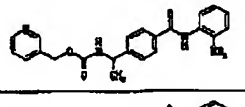
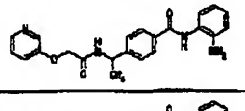
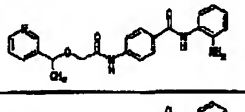
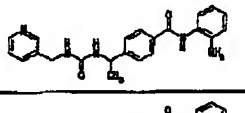
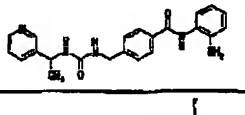
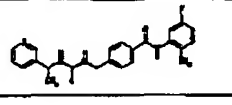
【0101】

【表28】表－3続きの1

11	
12	
13	
14	
15	
16	

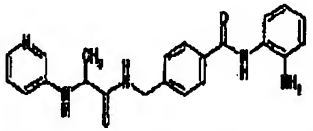
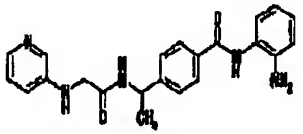
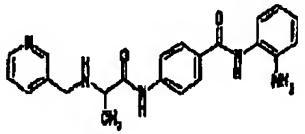
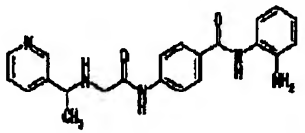
【0102】

【表29】表－4

1	
2	
3	
4	
5	
6	
7	
8	
9	
10	

【0103】

【表30】表−4続きの1

化合物番号	構造式
11	
12	
13	
14	

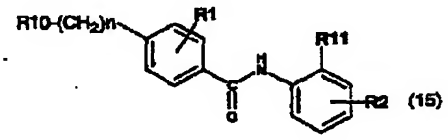
(0104)
The compound of this invention is able to be produced by for example following process.
[a] Formula (14) (formula 27).

(0105)

A-X-R9 (14)

[in the formula, A and X have the same said meanings. R9 is -C(=G) OH (G denotes oxygen atom or sulphur atom) or -NH2] and the compound represented by formula (15) (formula 28).

(0106)



(15)

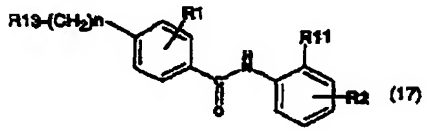
[in the formula, R1, R2 and n have the same said meanings. When R9 is -C(=G) OH (G has the same said meanings), R10 is -NH2, and when R9 is -NH2, R10 is -C(=G) OH (G has the same said meanings), R11 is protected amino group protected with protecting group used in conventional peptide synthesis such as tert-butoxy carbonyl group, or protected hydroxy group protected with protecting group used in conventional peptide synthesis such as benzyl group] are subjected to condensation reaction or,
[b] Formula (16) (formula 29).

(0107)
(formula 29)

A-X-R12 (16)

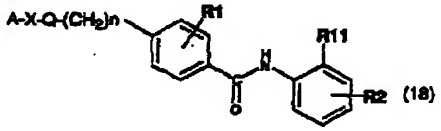
[In the formula, A and X have the same said meanings. R12 denotes -OH or-NH2] and the compound represented by formula (17) (formula 30) .

(0108)
(formula 30)



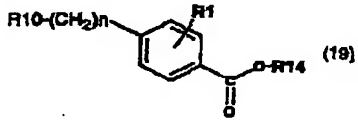
[In the formula, R1, R2, R11 and n have the same said meanings. R13 is -OH or -NH2.] are subjected to condensation reaction using N,N-carbonyldiimidazole, N,N-thiocarbonyl di imidazole, phosgene or thiophosgene, and the obtained compound represented by (18) (formula 31)

(0109)
(formula 31)



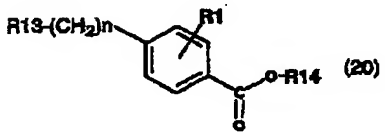
[In the formula, A, X, Q, n, R1, R2 and R11 have the same said meanings], is eliminated of protecting groups of the compound, and the compound of this invention can be obtained.
[c] The compound represented by formula (14) and formula (19) (formula 32).

(0110)
(formula 32)



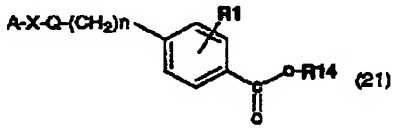
[In the formula, R1, R10 and n have the same said meanings. R14 is methyl group, ethyl group or tert-butyl group] are subjected to condensation reaction or,
[d] the compound represented by formula (16) and formula (20) (formula 33)

(0111)
(formula 33)



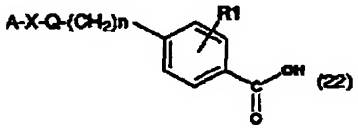
[In the formula, R1, R13, R14 and n have the same said meanings.] are subjected to condensation reaction using N,N-carbonyldiimidazole, N,N-thiocarbonyl di imidazole, phosgene or thiophosgene, and the obtained compound represented by formula (21) (formula 34).

(0112)
(formula 34)



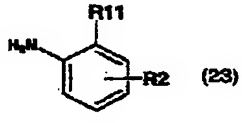
[In the formula, A, X, Q, n, R1 and R14 have the same said meanings], is hydrolysed, and the obtained compound represented by formula (22) (formula 35)

(0113)
(formula 3 5)



[In the formula, A, X, Q, n and R1 have the same said meanings] and the compound represented by formula (23) (formula 36).

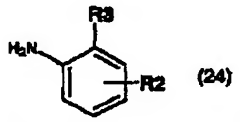
(0114)
(formula 36)



[In the formula, R2 and R11 have the same said meanings] are subjected to condensation reaction, and protecting group of the obtained compound represented by formula (18) is eliminated, thereby the compound of this invention can be obtained.

[e] The compound represented by formula (22) and formula (24) (formula 37).

(0115)
(formula 37)

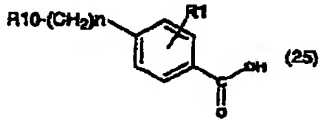


(24)

[In the formula, R2 and R3 have the same said meanings] are subjected to condensation reaction, thereby the compound of this invention can be obtained.

(0116)
Synthesis of typical intermediates are described. As for the compound represented by formula (15), the benzoic acid derivative represented by formula (25) (formula 38).

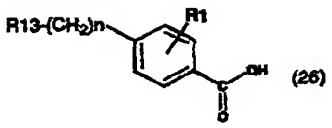
(0117)
(formula 38)



(25)

[In the formula, R1, R10 and n have the same said meanings] is introduced with suitable protecting group, thereafter are subjected to condensation reaction with the compound represented by formula (23), furthermore, deprotection is carried out, and thereby it can be obtained. As for the compound represented by formula (17), the benzoic acid derivative represented by formula (26) (formula 39).

(0118)
(formula 39)



(26)

[In the formula, R1, R13 and n have the same said meanings] is introduced with suitable protecting group, thereafter are subjected to condensation reaction with the compound represented by formula (23), furthermore, deprotection is carried out, and thereby it can be obtained. The compound represented by formula (23) can be obtained by introducing protecting group into the compound represented by formula (24).

(0119)

Thereafter reaction is described. Condensation reaction of [a] can be put into effect by amide bond forming reaction in ordinary peptide, for example process of active ester or mixed acid anhydride or acid chloride. For example, carboxylic acid component [a compound represented by formula (14) wherein R9 is -C(= G)OH (G has the same said meanings) or a compound represented by formula (15) wherein R10 is -C(= G)OH (G has the same said meanings)] and phenols such as 2,4,5-trichlorophenol, pentachlorophenol or 4-nitrophenol and the like or N-hydroxy compound such as N-hydroxysuccinimide, N-hydroxybenzotriazole and the like are condensed in the presence of dicyclohexylcarbodiimide, thereby it is converted into active ester, and thereafter it can be carried out by condensation with amine component [a compound represented by formula (14) wherein R9 is -NH2 or a compound represented by formula (15) wherein R10 is -NH2].

(0120)

Moreover, it can be carried out by reacting carboxylic acid [a compound represented by formula (14) wherein R9 is -C(= G)OH (G has the same said meanings) or a compound represented by formula (15) wherein R10 is -C(= G)OH (G has the same said meanings)] with oxalyl chloride, thionyl chloride, phosphorus oxychlorides and the like, thereby converting into acid chloride, and thereafter condensing with amine component [a compound represented by formula (14) wherein R9 is -NH2 or a compound represented by formula (15) wherein R10 is -NH2].

(0121)

Moreover, it can be carried out by reacting carboxylic acid component [a compound represented by formula (14) wherein R9 is -C(= G)OH (G has the same said meanings) or a compound represented by formula (15) wherein R10 is -C(= G)OH (G has the same said meanings)] with isobutyl chlorocarbonate, methanesulphonyl chloride or p-nitrobenzene sulphonyl chloride and the like, thereby obtaining mixed acid anhydride, and thereafter condensing with amine component [a compound represented by formula (14) wherein R9 is -NH2 or a compound represented by formula (15) wherein R10 is -NH2].

(0122)
Furthermore, aforesaid condensation reaction can be carried out by using peptide condensation reagent alone such as dicyclohexylcarbodiimide, N,N-carbonyldiimidazole, diphenyl phosphoric acid azide, diethyl phosphoric acid cyanide, 2-chloro-1,3-dimethyl imidazoloninum chloride and the like.

(0123)
The reaction is carried out at -20 to +50 degrees usually for 30 minutes to 48 hours. As the solvent used, for example, alcohols such as methanol, ethanol and the like or a mixture thereof are nominated in addition to aromatic hydrocarbon species such as benzene, toluene and the like, ethers such as tetrahydrofuran, dioxane, diethyl ether and the like, halogenated hydrocarbons such as methylene chloride, chloroform and the like, N,N-dimethylformamide. In accordance with requirements organic base for example triethylamine or pyridine is added and is reacted.

(0124)
Condensation reaction of [b] can be put into effect by activating either of the compound represented by formula (16) or formula (17) using phosgene, thiophosgene, N,N-carbonyldiimidazole and N,N'-thiocarbonyl di imidazole and the like, thereafter by reacting with the other compound. The reaction is carried out at -20 to +50 degrees usually for 30 minutes to 48 hours. As the solvent used, for example, aromatic hydrocarbon species such as benzene, toluene and the like, ethers such as tetrahydrofuran, dioxane, diethyl ether and the like, halogenated hydrocarbons such as methylene chloride, chloroform and the like, N,N-dimethylformamide or a mixture thereof are nominated. In accordance with requirements organic base for example triethylamine or pyridine is added and is reacted.

(0125)
Condensation reaction of [c] can be performed by process same as in condensation reaction of [a]. Condensation reaction of [d] can be carried out by process same as in condensation reaction of [b].

(0126)
Elimination of protecting groups of the compound represented by formula (17) is performed under conditions to be used in ordinary peptide forming reaction. For example, when R11 is an amino group protected with t-butoxycarbonyl group in formula (18), deprotecting reaction can be carried out by treating with acid such as hydrochloric acid or trifluoroacetic acid.

(0127)
Salt of the compound represented by formula (1) and formula (13) can be obtained by reaction to produce compound represented by formula (1) and formula (13), but the salt can be easily formed with pharmacologically acceptable acid. As acid thereof, for example inorganic acid such as hydrochloric acid, hydrobromic acid, sulphuric acid, orthophosphoric acid and organic acid such as acetic acid, tartaric acid, fumaric acid, maleic acid, citric acid, benzoic acid, trifluoroacetic acid, p-toluenesulphonic acid are nominated. These salts can also be used as the effective ingredient compound of this invention in the same way as in the free form of the compound of formula (1) and formula (13).

(0128)
The compound represented by formula (1) and formula (13) can be isolated and purified from the reaction mixture by ordinary separation means, for example process such as extraction, recrystallisation method, column chromatography.

(0129)
Novel benzamide derivatives and novel anilide derivatives of this invention have differentiation induction action and are useful as therapy and/or improvement agent for malignant tumour, autoimmune disease, dermatopathia, parasite infestation.

(0130)

Wherein, as malignant tumour, in addition to hematopoietic organ tumours such as acute leukaemia, chronic leukaemia, malignancy lymphoma, multiple myeloma, macroglobulinemia, solid tumours such as colon cancer, brain tumour, head cervix cancer, breast cancer, lung cancer, cancer of the oesophagus, gastric cancer, hepatoma, gallbladder cancer, bile duct cancer, pancreatic carcinoma, insula pancreatica cell cancer, kidney cell cancer, adrenal cortex cancer, tumour of the urinary bladder, prostatic cancer, testis tumour, ovary cancer, uterine cancer, carcinoma villosum, cancer of the thyroid, bad carcinoid tumour, skin cancer, malignant melanoma, osteosarcoma, soft tissue sarcoma, neuroblastoma, Wilms tumour, retinoblastoma are nominated.

(0131)
As autoimmune disease, rheumatism, nephritis, diabetes mellitus, systemic lupus erythematosus, human autoimmune lymphocytotic lymphadenopathy, immunoblastic lymphadenopathy, Crohn's disease, ulcerative colitis are nominated. As dermatopathia, psoriasis, acne, eczema, atopic dermatitis, parasitic dermatosis, alopecia, pyogenic dermatosis, skin sclerosis are nominated. As parasite infestation, a disease caused by infection of parasite such as malaria infection is denoted. Moreover target disease of this invention does not need to be restricted to these.

(0132)
The effective ingredient compounds of this invention are useful as drug, and these are used in a form of general medical formulation. Formulation is prepared using diluent of for example filler, expander, binding agent, moisturising agent, disintegrating agent, surface active agent, lubricant or excipient which are usually used. As this drug formulation, various forms can be selected corresponding to the therapy object and as representative thereof, tablet, pill, powder, liquid medicine, suspending agent, emulsion, granule, capsule agent, injection (liquid medicine, suspending agent) and suppository and the like are nominated.

(0133)
When it is formed into a tablet, various ones which is known well in the prior art as a carrier in this sphere, can be widely used. As example thereof, for example excipient such as lactose, dextrose, starch, calcium carbonate, kaolin, crystalline cellulose, silicic acid, and the like, binding agent such as water, ethanol, propyl alcohol, single syrup, dextrose liquid, starch liquid, gelatine solution, carboxymethyl cellulose, shellac, methyl cellulose, polyvinylpyrrolidone and the like,

disintegrating agent such as dried starch, sodium alginate, agar powder, carmellose calcium, starch, lactose, disintegration depressant such as refined sugar,

(0134)
cacao butter, hydrogenation oil, absorption promoter such as quaternary ammonium salt group, sodium lauryl sulphate and the like, moisturising agent such as glycerine, starch and the like, adsorbent such as starch, lactose, kaolin, bentonite, colloidal silicic acid, lubricant such as talc, stearate, polyethyleneglycol and the like can be used. Furthermore, as for a tablet, it can be made into coated tablet of ordinary agent in accordance with requirements, for example sugar coated tablet, gelatine encapsulation tablet, enteric-coated encapsulation tablet, film coating tablet or bilayer tablet, multilayer tablet.

(0135)
When it is formed into pill, ones well known in prior art in this sphere as a carrier, can be widely used. As example thereof, for example excipients such as crystalline cellulose, lactose, starch, hardening vegetable oil, kaolin, talc and the like, binding agent such as powdered gum Arabic, tragacanth powder, gelatine and the like, disintegrating agent such as carmellose calcium, agar and the like are nominated.

(0136)
Capsule agent is prepared by mixing the effective ingredient compound with above-mentioned various carriers according to conventional method, and packing into hard gelatine capsule, soft capsule and the like.

(0137)
When it is prepared as injection, it is preferred that liquid medicine, emulsion and suspending agent are sterilised and are isotonic with blood, and when it is formed into these, ones conventionally used in prior art in this sphere as diluent, for example water, ethanol, macrogol, propylene glycol, ethoxylation isostearyl alcohol, polyoxyisosteary alcohol, polyoxyethylene sorbitan fatty acid ester species can be used. In this case, sodium chloride, dextrose or glycerine of necessary quantity may be contained in drug formulation to prepare an isotonic solution, and moreover ordinary solubiliser, buffer agent, analgesic and the like may be added.

(0138)
When it is formed into suppository, ones well known in prior art as a carrier can be widely used. As example thereof, for example semi-synthetic glyceride, cacao butter, esters of higher alcohol, higher alcohol, polyethyleneglycol and the like are nominated.

(0139)
Furthermore colorant, preservative, flavour, flavour agent, sweetener and other drug can be contained in the drug formulation in accordance with requirements. The quantity of the effective ingredient compound which should be contained in these drug formulations of this invention is not restricted in particular and suitably selected from a wide range, but it is usually about 1-70 wt.% and preferably made into about 5-50 wt.% in the formulation composition.

(0140)
As for the administration method of these drug formulation of this invention, there are no restrictions in particular and it is administered by the methods that suits various formulation, age of patient, sex, degree of disease and other conditions. For example, in the cases of tablet, pill, liquid medicine, suspending agent, emulsion, granule and capsule agent, it is orally-administered, and in the case of injection, it is administered intravenously by itself or by being mixed with ordinary fluid replacement such as glucose, amino acid, and furthermore it is administered intramuscularly, subcutaneously or intraperitoneously by itself in accordance with requirements. In the case of suppository, it is administered in rectum.

(0141)
Dosage of these drug formulation of this invention is suitably selected by application, age of patient, sex, degree of disease and other conditions, but it is usually made into about around 0.0001-100 mg as the quantity of the effective ingredient compound per day per 1 kg weight. Moreover, it is desirable that the effective ingredient compound is contained by about 0.001-1,000 mg range in the formulation of administration unit form. The compound and salts thereof represented by formula (1) and formula (13) of this invention do not demonstrate toxicity that can cause a problem in dosage that demonstrates pharmacological effect.

(0142)
(Example)

Below this invention is described in greater detail with Examples, but this invention is not restricted to these. Moreover number in brackets of title is the number of the compound exemplified in Detailed Description.

(0143)

Example 1.

Synthesis of N-(2-aminophenyl)-4-(N-benzoylamino methyl) benzamide hydrochloride (Table-1: hydrochloride of compound number 1).

(1-1) Triethylamine 42 ml (300 mmol) were added to dichloromethane (450 ml) suspension of 4-aminomethyl benzoic acid 21.16 g (140 mmol). Dichloromethane (50 ml) solution of anhydrous trifluoroacetic acid 60.4 g (287 mmol) was dropwise added while maintaining an internal temperature at 3-8 degrees under ice cooling, thereafter the mixture was stirred for three hours. The reaction liquor was introduced into saturated aqueous sodium bicarbonate, thereafter furthermore it was acidified with 10 % hydrochloric acid aqueous solution. Precipitated gel state precipitate was recovered by filtration, and, by drying, 4-(N-trifluoroacetylamino methyl) benzoic acid 30.4 g (yield 87.8 %) were obtained as the milk-white solid.

1H NMR (270 MHz, DMSO-d6) delta ppm: 4.47 (2H, d, J = 5.8 Hz), 7.39 (2H, d, J = 8.1 Hz), 7.93 (2H, d, J = 8.1 Hz), 10.08 (1H, t, J = 5.8 Hz), 12.95 (1H, br.s).

(0144)

(1-2) 1N sodium hydroxide aqueous solution (500 ml) was added to dioxane (1000 ml) solution of o-phenylenediamine 108 g (1.0 mol), and dioxane (500 ml) solution of di tert-butyl di carbonate 218 g (mol 1.1) was added under ice cooling. The mixture was stirred at room temperature for six hours, thereafter left to stand overnight. The solvent was concentrated to 1/2 vol and it was extracted with ethyl acetate. Organic layer was washed with saturated aqueous sodium chloride solution, and thereafter it was dried, and the obtained residue from which the solvent was eliminated by distillation, was refined by silica gel column chromatography (chloroform), and N-tert-butoxycarbonyl-o-phenylenediamine 68.4 g (yield 32.8 %) were obtained as white solid by washing the obtained solid with ethyl ether.

1H NMR (270 MHz, CDCl3) delta ppm: 1.51 (9H, s), 3.75 (2H, s), 6.26 (1H, s), 6.77 (1H, d, J = 8.1 Hz), 6.79 (1H, dd, J = 7.3, 8.1 Hz), 7.00 (1H, dd, J = 7.3, 8.1 Hz), 7.27 (1H, d, J = 8.1 Hz).

(0145)

(1-3) Oxalyl chloride 21 g (165 mmol) were gradually added dropwise to dichloromethane (200 ml) suspension of compound 30.0 g (121 mmol) obtained in step (1-1) while being cooled with ice (internal temperature 10-15 degrees). During this, and DMF was added sometimes (by 0.1 ml for every 2 ml of dropwise addition). After total quantity of dropwise addition, the mixture was stirred till effervescence stopped, and thereafter the mixture was stirred for one hour at 40 degrees. The solvent was eliminated by distillation, and next, excess oxalyl chloride was formed into an azeotrope with toluene. Next, it was dissolved in dichloromethane (100 ml) once again. Into dichloromethane (100 ml)-pyridine (200 ml) solution of compound 22.88 g (110 mmol) obtained in Step (1-2), was dropwise added acid chloride solution prepared before under ice cooling (internal temperature 7-9 degrees).

(0146)

On completion of the dropwise addition it was warmed to room temperature, and next it was left to stand overnight. Saturated aqueous sodium bicarbonate was added to the reaction mixture, and thereafter it was extracted with chloroform, and it was washed with saturated aqueous sodium chloride solution, and thereafter it was dried, and the solvent was eliminated by distillation. Methanol-diisopropyl ether was added to obtained residue, and the precipitated solid was recovered by filtration, and, by drying, N-(2-(N-tert-butoxycarbonyl) aminophenyl)-4-(N-trifluoroacetylamino methyl) benzamide 28.1 g (yield 58 %) were obtained as the straw-coloured solid.

1H NMR (270 MHz, DMSO-d6) delta ppm: 1.44 (9H, s), 4.48 (2H, d, J = 5.9 Hz), 7.12-7.23 (2H, m), 7.44 (2H, d, J = 8.1 Hz), 7.54 (2H, d, J = 8.1 Hz), 7.94 (2H, d, J = 8.1 Hz), 8.68 (1H, br.s), 9.83 (1H, s), 10.10 (1H, br.t, J = 5.9 Hz).

(0147)

(1-4) Potassium carbonate 4.70 g (34.0 mmol) were added to methanol (120 ml)-water (180 ml) suspension of compound 13.12 g (30 mmol) of step (1-3), and it was heated with stirring at 70 degC for four hours. It was extracted with chloroform, and organic layer was washed with saturated aqueous sodium chloride solution, and thereafter it was dried, and the solvent was eliminated by distillation, and 4-aminomethyl-N-(2-(N-tert-butoxycarbonyl) aminophenyl)

benzamide 10.3 g (quantitative) were obtained as the straw-coloured amorphous state solid by drying.

1H NMR (270 MHz, DMSO-d6) delta ppm: 3.80 (2H, s), 7.13-7.23 (2H, m), 7.48-7.58 (4H, m), 7.90 (2H, d, J = 8.1 Hz), 8.69 (1H, br.s), 9.77 (1H, br.s).

(0148)

(1-5) Benzoyl chloride 0.08 g (0.53 mmol) were added under ice cooling into pyridine (5 ml) solution of compound 0.11 g of step (1-4) (0.44 mmol) and thereafter were stirred for eight hours while gradually raising temperature to room temperature. Saturated aqueous sodium bicarbonate was added, thereafter it was extracted with ethyl acetate. Organic layer was washed with saturated aqueous sodium chloride solution and was dried, and the residue obtained by elimination by distillation of the solvent was washed with diisopropyl ether, and, by drying obtained solid, N-(2-(N-tert-butoxycarbonyl) aminophenyl)-4-(N-benzoylamino methyl) benzamide 0.14 g (yield 71.4 %) were obtained as white solid.

1H NMR (270 MHz, DMSO-d6) delta ppm: 1.44 (9H, s), 4.56 (2H, d, J = 5.9 Hz), 7.11-7.22 (2H, m), 7.46-7.56 (7H, m), 7.90-7.94 (4H, m), 8.67 (1H, s), 9.15 (1H, t, J = 5.9 Hz), 9.81 (1H, s).

(0149)

(1-6) 4 N hydrochloric acid-dioxane (5 ml) was added to dioxane (5 ml)-methanol (1 ml) solution of compound 0.10 g (0.224 mmol) of step (1-5) and was stirred at room temperature for seven hours. Diisopropyl ether was added to the residue obtained by elimination of the solvent, and obtained solid was recovered by filtration, and, by drying, N-(2-aminophenyl)-4-(N-benzoylamino methyl) benzamide hydrochloride 0.08 g (yield 93 %) were obtained as the pale-brown solid.

Mp. 206-209 deg C.

1H NMR (270 MHz, DMSO-d6) delta ppm: 4.57 (2H, d, J = 5.8 Hz), 7.27-7.38 (4H, m), 7.47-7.59 (5H, m), 7.92 (1H, d, J = 8.1 Hz), 8.05 (1H, d, J = 8.1 Hz), 9.19 (1H, t, J = 5.8 Hz), 10.38 (1H, br.s).

IR (KBr) cm-1 = 3286, 3003 (br.), 1630, 1551, 1492, 1306, 1250, 749, 695.

By process same as in Example 1, the compounds of Example 2 to Example 44 were synthesised. Below melting point (mp.) of the compound, 1H NMR, measured values of IR are shown.

(0150)
Example 2.
N-(2-aminophenyl)-4-(N-(2-chlorobenzoyl) aminomethyl) benzamide (Table-1: compound number 14).

Mp. 201-204 deg C (dec.).
1H NMR (270 MHz, DMSO-d6) delta ppm: 4.52 (2H, t, J = 5.9 Hz), 4.89 (2H, br.s), 6.60 (1H, ddd, J = 1.5, 7.3, 8.1 Hz), 6.78 (1H, dd, J = 1.5, 8.1 Hz), 6.97 (1H, ddd, J = 1.5, 7.3, 8.1 Hz), 7.17 (1H, d, J = 8.1 Hz), 7.38-7.54 (6H, m), 7.97 (2H, d, J = 8.1 Hz), 9.06 (1H, br.t, J = 5.9 Hz), 9.63 (1H, br.s).
IR (KBr) cm-1 = 3268, 1649, 1458, 1304, 748.

(0151)
Example 3.
N-(2-aminophenyl)-4-(N-(2-nitrobenzoyl) aminomethyl) benzamide hydrochloride (hydrochloride of Table-1 = compound number 18).

Mp. 210-212 deg C (dec.).
1H NMR (270 MHz, DMSO-d6) delta ppm: 4.55 (2H, t, J = 5.9 Hz), 7.20-7.40 (3H, m), 7.50-7.60 (1H, m), 7.53 (2H, d, J = 8.1 Hz), 7.60-7.70 (2H, m), 7.83 (1H, ddd, J = 1.5, 8.1, 8.1 Hz), 8.00-8.10 (3H, m), 9.34 (1H, t, J = 5.9 Hz), 10.43 (1H, br.s).
IR (KBr) cm-1 = 3283, 2500-3000 (br.), 1648, 1534, 1461, 1362, 1314, 754, 701.

(0152)
Example 4.
N-(2-aminophenyl)-4-(N-(4-methylbenzoyl) aminomethyl) benzamide hydrochloride (hydrochloride of Table-1 = compound number 28).

Mp. (amorphous).

1H NMR (270 MHz, DMSO-d6) delta ppm: 2.37 (3H, s), 4.56 (2H, d, J = 5.0 Hz), 7.20-7.30 (6H, m), 7.47 (4H, d, J = 8.8 Hz), 7.82 (2H, d, J = 8.8 Hz), 8.03 (2H, d, J = 8.8 Hz), 9.09 (1H, t, J = 5 Hz), 10.36 (1H, br.s).
IR (KBr) cm-1 = 3269 (br.), 2861 (br.), 1743, 1636, 1534, 1505, 1456, 1308, 1120, 753.

(0153)
Example 5.
N-(2-aminophenyl)-4-(N-(3-methoxybenzoyl) aminomethyl) benzamide (Table-1 = compound number 30).

Mp. 182-185 deg C.
1H NMR (270 MHz, DMSO-d6) delta ppm: 3.81 (3H, s), 4.54 (2H, d, J = 5.9 Hz), 4.88 (2H, br.s), 6.60 (1H, dd, J = 6.6, 7.3 Hz), 6,78 (1H, d, J = 7.3 Hz), 6.97 (1H, dd, J = 6.6, 7.3 Hz), 7.11 (1H, dd, J = 1.5, 8.1 Hz), 7.16 (1H, d, J = 7.3 Hz), 7.35-7.51 (5H, m), 7.94 (2H, d, J = 8.1 Hz), 9.12 (1H, br.t, J = 5.9 Hz), 9.63 (1H, br.s).
IR (KBr) cm-1 = 3301, 1637, 1524, 1489, 1457, 1314, 1248, 752.

(0154)
Example 6.
N-(2-aminophenyl)-4-(N-(4-methoxybenzoyl) aminomethyl) benzamide (Table-1 = compound number 31).

Mp. 149-151 deg C.
1H NMR (270 MHz, DMSO-d6) delta ppm: 3.82 (3H, s), 4.53 (2H, d, J = 5.9 Hz), 4.88 (2H, s), 6.59 (1H, dd, J = 7.3, 7.3 Hz), 6.77 (1H, d, J = 8.1 Hz), 6.94-7.00 (1H, m), 7.02 (2H, d, J = 8.8 Hz), 7.16 (1H, d, J = 8.1 Hz), 7.43 (2H, d, J = 8.1 Hz), 7.89 (2H, d, J = 8.8 Hz), 7.94 (2H, d, J = 8.1 Hz), 8.98 (1H, br.t, J = 5.9 Hz), 9.61 (1H, br.s).
IR (KBr) cm-1 = 3297, 1630, 1527, 1505, 1457, 1256, 1177, 1024, 843, 749.

(0155)
Example 7.
N-(2-aminophenyl)-4-(N-(3, 4,5-trimethoxy benzoyl) aminomethyl) benzamide (Table-1 = compound number 33).

Mp. 208-210 deg C (dec.).
1H NMR (270 MHz, DMSO-d6) delta ppm: 3.71 (3H, s), 3.83 (6H, s), 4.55 (2H, d, J = 5.9 Hz), 4.88 (2H, br.s), 6.60 (1H, dd, J = 7.3, 8.1 Hz), 6.78 (1H, d, J = 8.1 Hz), 6.97 (1H, dd, J = 6.6, 8.1 Hz), 7,16 (1H, d, J = 8.1 Hz), 7.26 (2H, s), 7.44 (2H, d, J = 8.1 Hz), 7.95 (2H, d, J = 8.8 Hz), 9.07 (1H, t, J = 5.9 Hz), 9.62 (1H, br.s).
IR (KBr) cm-1 = 3267, 1635, 1582, 1457, 1237, 1132, 755.

(0156)
Example 8.
N-(2-aminophenyl)-4-(N-(3,4,5-trimethoxybenzoyl) aminomethyl) benzamide (Table-1 = compound number 36).

Mp. 216-219 deg C (dec.).
1H NMR (270 MHz, DMSO-d6) delta ppm: 2.98 (6H, s), 4.51 (2H, d, J = 5.9 Hz), 4.88 (2H, br.s), 6.60 (1H, dd, J = 8.1, 8.1 Hz), 6.71 (2H, d, J = 8.8 Hz), 6.97 (1H, dd, J = 7.3, 8.1 Hz), 7.16 (1H, d, J = 7.3 Hz), 7.41 (2H, d, J = 8.1 Hz), 7.78 (2H, d, J = 8.8 Hz), 7.93 (2H, d, J = 8.1 Hz), 8.77 (1H, t, J = 5.9 Hz), 9.63 (1H, br.s).
IR (KBr) cm-1 = 3301, 1632, 1519, 1457, 1298, 754.

(0157)
Example 9.
N-(2-aminophenyl)-4-(N-(4-trifluoromethyl benzoyl) aminomethyl) benzamide (Table-1 = compound number 42).

Mp. 243-246 deg C.
1H NMR (270 MHz, DMSO-d6) delta ppm: 4.58 (2H, d, J = 5.9 Hz), 4.88 (2H, br.s), 6.59 (1H, dd, J = 6.6, 7.3 Hz), 6.77 (1H, d, J = 8.1 Hz), 6.94 (1H, dd, J = 5.9, 6.6 Hz), 7.16 (1H, d, J = 8.1 Hz), 7.45 (2H, d, J = 8.1 Hz), 7.88 (2H, d, J = 8.8 Hz), 7.95 (2H, d, J = 8.1 Hz), 8.11 (2H, d, J = 8.1 Hz), 9.38 (1H, t, J = 5.9 Hz), 9.64 (1H, br.s).
IR (KBr) cm-1 = 3301, 1640, 1549, 1523, 1458, 1334, 1162, 1120, 1070, 856, 750.

(0158)

Example 10.

N-(2-aminophenyl)-4-(N-(4-carboxy benzoyl) aminomethyl) benzamide hydrochloride (hydrochloride of Table-1 = compound number 45).

Mp. (amorphous).

1H NMR (270 MHz, DMSO-d6) delta ppm: 4.58 (2H, d, J = 5.9 Hz), 7.29-7.37 (3H, m), 7.49 (3H, d, J = 8.1 Hz), 8.02-8.06 (6H, m), 9.36 (1H, t, J = 5.9 Hz), 10.4 (1H, br.s).

IR (KBr) cm-1 = 3432 (br.), 1718, 1637, 1542, 1499, 1303 (br.), 1116, 1018, 757.

(0159)

Example 11.

N-(2-aminophenyl)-4-(N-(4-methoxycarbonyl benzoyl) aminomethyl) benzamide (Table-1 = compound number 46).

Mp. 204-209 deg C (dec.).

1H NMR (270 MHz, DMSO-d6) delta ppm: 3.89 (3H, s), 4.57 (2H, d, J = 5.9 Hz), 4.88 (2H, br.s), 6.60 (1H, dd, J = 6.6, 7.3 Hz), 6.78 (2H, d, J = 7.3 Hz), 6.97 (1H, ddd, J = 1.5, 6.6, 7.3 Hz), 7.16 (1H, d, J = 7.3 Hz), 7.45 (2H, d, J = 8.1 Hz), 7.95 (2H, d, J = 8.1 Hz), 8.03 (2H, d, J = 8.8 Hz), 8.07 (2H, d, J = 8.8 Hz), 9.35 (1H, t, J = 5.9 Hz), 9.64 (1H, br.s).

IR (KBr) cm-1 = 3287 (br.), 1721, 1634, 1281, 1113, 750, 703.

(0160)

Example 12.

N-(2-aminophenyl)-4-(N-picolinoyl aminomethyl) benzamide (Table-1 = compound number 173).

Mp. 173-178 deg C (dec.).

1H NMR (270 MHz, DMSO-d6) delta ppm: 4.57 (2H, d, J = 6.6 Hz), 4.88 (2H, br.s), 6.59 (1H, dd, J = 7.3, 8.1 Hz), 6.77 (1H, d, J = 8.1 Hz), 6.96 (1H, dd, J = 7.3, 8.1 Hz), 7.16 (1H, d, J = 7.3 Hz), 7.44 (2H, d, J = 8.1 Hz), 7.60-7.65 (1H, m), 7.93 (2H, d, J = 8.1 Hz), 7.98-8.08 (2H, m), 8.67 (1H, d, J = 4.4 Hz), 9.45 (1H, t, J = 6.6 Hz), 9.61 (1H, br.s).

IR (KBr) cm-1 = 3330, 1656, 1634, 1523, 1456, 1294, 752.

(0161)

Example 13.

N-(2-aminophenyl)-4-(N-(6-methyl picolinoyl) aminomethyl) benzamide (Table-1 = compound number 178).

Mp. 172-173 deg C.

1H NMR (270 MHz, DMSO-d6) delta ppm: 2.51 (3H, s), 4.57 (2H, d, J = 6.6 Hz), 5.0 (2H, br.s), 6.61 (1H, dd, J = 7.3, 8.1 Hz), 6.79 (1H, d, J = 7.3 Hz), 6.98 (1H, dd, J = 7.3, 8.1 Hz), 7.17 (1H, d, J = 7.3 Hz), 7.44 (2H, d, J = 8.1 Hz), 7.43-7.49 (1H, m), 7.84-7.90 (2H, m), 7.94 (2H, d, J = 8.1 Hz), 9.27 (1H, t, J = 5.9 Hz), 9.64 (1H, br.s).

IR (KBr) cm-1 = 3331, 1675, 1634, 1594, 1523, 1454, 1307, 1292, 750.

(0162)

Example 14.

N-(2-aminophenyl)-4-(N-nicotinoyl aminomethyl) benzamide (Table-1 = compound number 71).

Mp. 193-196 deg C.

1H NMR (270 MHz, DMSO-d6) delta ppm: 4.58 (2H, d), 4.88 (2H, br.s), 6.60 (1H, t), 6.78 (1H, d), 6.97 (1H, t), 7.16 (1H, d), 7.46 (2H, d), 7.53 (1H, dd), 7.95 (2H, d), 8.24 (1H, ddd), 8.73 (1H, dd), 9.07 (1H, d), 9.32 (1H, br.t), 9.63 (1H, br.s).

IR (KBr) cm-1 = 3301, 1639, 1522, 1457, 1314, 749, 705.

(0163)

Example 15.

N-(2-aminophenyl)-4-(N-(2-methyl nicotinoyl) aminomethyl) benzamide (Table-1 = compound number 141).

Mp. 191-194 deg C (dec.).

1H NMR (270 MHz, DMSO-d6) delta ppm: 2.53 (3H, s), 4.53 (2H, d, J = 5.9 Hz), 4.88 (2H, br.s), 6.60 (1H, dd, J = 6.6, 8.1 Hz), 6.78 (1H, d, J = 7.3 Hz), 6.97 (1H, dd, J = 7.3, 8.1 Hz), 7.17 (1H, d, J = 7.3 Hz), 7.29 (1H, dd, J = 5.1, 8.1 Hz), 7.47 (2H, d, J = 8.1 Hz), 7.77 (1H, dd, J = 1.5, 8.1 Hz), 7.97 (2H, d, J = 8.1 Hz), 8.51 (1H, dd, J = 1.5, 5.1 Hz), 9.06 (1H, t, J = 5.9 Hz), 9.64 (1H, s).

IR (KBr) cm-1 = 3261, 1642, 1523, 1310, 753.

(0164)

Example 16.

N-(2-aminophenyl)-4-(N-(6-methyl nicotinoyl) aminomethyl) benzamide (Table-1 = compound number 143).

Mp. 186-190 deg C (dec.).

1H NMR (270 MHz, DMSO-d6) delta ppm: 2.36 (3H, s), 4.56 (2H, d, J = 5.9 Hz), 4.88 (2H, s), 6.60 (1H, dd, J = 7.4, 7.8 Hz), 6.78 (1H, d, J = 7.8 Hz), 6.97 (1H, dd, J = 6.9, 6.9 Hz), 7.16 (1H, d, J = 7.4 Hz), 7.37 (1H, d, J = 8.3 Hz), 7.45 (2H, d, J = 8.3 Hz), 7.95 (2H, d, J = 8.3 Hz), 8.13 (1H, dd, J = 2.0, 8.3 Hz), 8.96 (1H, s), 9.24 (1H, t, J = 5.9 Hz), 9.63 (1H, br.s).

IR (KBr) cm-1 = 3302, 1636, 1602, 1523, 1489, 1457, 1313, 751.

(0165)

Example 17.

N-(2-aminophenyl)-4-(N-(2-chloro nicotinoyl) aminomethyl) benzamide (Table-1 = compound number 154).

Mp. 176-178 deg C (dec.).

1H NMR (270 MHz, DMSO-d6) delta ppm: 4.54 (2H, t, J = 5.9 Hz), 4.90 (2H, br.s), 6.60 (1H, ddd, J = 1.5, 7.3, 7.3 Hz), 6.78 (1H, d, J = 8.1 Hz), 6.97 (1H, ddd, J = 1.5, 7.3, 7.3 Hz), 7.18 (1H, d, J = 8.1 Hz), 7.48-7.54 (3H, m), 7.94-7.99 (3H, m), 8.49 (1H, dd, J = 2.1, 5.1 Hz), 9.23 (1H, br.t, J = 5.9 Hz), 9.65 (1H, br.s).

IR (KBr) cm-1 = 3264, 1649, 1524, 1400, 1309, 751.

(0166)

Example 18.

N-(2-aminophenyl)-4-(N-(6-chloro nicotinoyl) aminomethyl) benzamide (Table-1 = compound number 156).

Mp. 205-208 deg C (dec.).

1H NMR (270 MHz, DMSO-d6) delta ppm: 5.57 (2H, d, J = 5.9 Hz), 6.60 (1H, dd, J = 7.3, 7.3 Hz), 6.78 (1H, d, J = 8.1 Hz), 6.96 (1H, dd, J = 7.3, 8.1 Hz), 7.16 (1H, d, J = 8.1 Hz), 7.45 (2H,

d, J = 8.1 Hz), 7.66 (1H, d, J = 8.8 Hz), 7.95 (2H, d, J = 8.1 Hz), 8.27-8.32 (1H, m), 8.90 (1H, d, J = 2.1 Hz), 9.38 (1H, t, J = 5.9 Hz), 9.63 (1H, s).
IR (KBr) cm-1 = 3318 (br.), 2929, 1646, 1590, 1525, 1503, 1454, 1108, 745.

(0167)
Example 19.
N-(2-aminophenyl)-4-(N-iso nicotinoyl aminomethyl) benzamide (Table-1 = compound number 183).

Mp. 234-237 deg C (dec.).
1H NMR (270 MHz, DMSO-d6) delta ppm: 4.57 (2H, t, J = 5.9 Hz), 4.88 (2H, br.s), 6.59 (1H, dd, J = 6.6, 7.3 Hz), 6.78 (1H, d, J = 8.1 Hz), 6.96 (1H, dd, J = 7.3, 7.3 Hz), 7.16 (1H, d, J = 7.3 Hz), 7.45 (2H, d, J = 8.1 Hz), 7.81 (2H, d, J = 1.5, 4.4 Hz), 7.95 (2H, d, J = 8.1 Hz), 8.75 (2H, d, J = 6.6 Hz), 9.41 (1H, t, J = 5.9 Hz), 9.62 (1H, br.s).
IR (KBr) cm-1 = 3298, 1646, 1550, 1525, 1457, 1304, 843, 760, 695.

(0168)
Example 20.
N-(2-aminophenyl)-4-(N-(pyrazin-2-yl) carbonylamino methyl) benzamide (Table-1 = compound number 191).
Mp. 207 deg C (dec.).
1H NMR (270 MHz, DMSO-d6) delta ppm: 4.58 (2H, d, J = 5.9 Hz), 4.88 (2H, br.s), 6.59 (1H, dd, J = 7.3, 7.3 Hz), 6.77 (1H, d, J = 8.1 Hz), 6.94 (1H, ddd, J = 1.5, 7.3, 8.1 Hz), 7.15 (1H, d, J = 7.3 Hz), 7.45 (2H, d, J = 8.1 Hz), 7.93 (2H, d, J = 8.1 Hz), 8.77 (1H, d, J = 1.5 Hz), 8.90 (1H, d, J = 2.1 Hz), 9.21 (1H, s), 9.55-9.61 (2H, m).
IR (KBr) cm-1 = 3368 (br.), 1657, 1524, 1455, 1295, 1023, 751.

(0169)
Example 21.
N-(2-aminophenyl)-4-(N-(thiophen-2-yl) carbonylamino methyl) benzamide (Table-1 = compound number 201).

Mp. 202-205 deg C (dec.).

1H NMR (270 MHz, DMSO-d6) delta ppm: 4.52 (2H, t, J = 5.9 Hz), 4.88 (2H, br.s), 6.60 (1H, dd, J = 6.6, 7.3 Hz), 6.78 (1H, d, J = 8.1 Hz), 6.97 (1H, dd, J = 7.3, 8.1 Hz), 7.15-7.18 (2H, m), 7.43 (2H, d, J = 8.1 Hz), 7.78 (1H, d, J = 4.4), 7.82 (1H, d, J = 3.7 Hz), 7.95 (2H, d, J = 8.1 Hz), 9.12 (1H, br.t, J = 5.9 Hz), 9.62 (1H, br.s).
IR (KBr) cm-1 = 3306, 1633, 1523, 1456, 1297, 750, 716.

(0170)
Example 22.
N-(2-aminophenyl)-4-(N-(furan-2-yl) carbonylamino methyl) benzamide (Table-1 = compound number 205).

Mp. 197 deg C (dec.).

(0171)
1H NMR (270 MHz, DMSO-d6) delta ppm: 4.59 (2H, d, J = 6.6 Hz), 4.86 (2H, br.s), 6.59 (1H, dd, J = 6.6, 6.6 Hz), 6.63 (1H, dd, J = 1.5, 3.6 Hz), 6.78 (1H, d, J = 8.1 Hz), 6.96 (1H, dd, J = 7.3, 6.6 Hz), 7.10-7.20 (2H, m), 7.41 (2H, d, J = 8.1 Hz), 7.84 (1H, s), 7.94 (2H, d, J = 8.1 Hz), 9.00 (1H, br.t, J = 5.9 Hz), 9.62 (1H, s).
IR (KBr) cm-1 = 3245, 1651, 1573, 1545, 1323, 1241, 745.

(0172)
Example 23.
N-(2-aminophenyl)-4-(N-(pyrrole-2-yl) carbonylamino methyl) benzamide (Table-1 = compound number 209).

Mp. 216-220 deg C (dec.).
1H NMR (270 MHz, DMSO-d6) delta ppm: 4.50 (2H, d, J = 5.9 Hz), 4.88 (2H, br.s), 6.10 (1H, dd, J = 2.1, 5.9 Hz), 6.59 (1H, dd, J = 7.3, 7.3 Hz), 6.77 (1H, dd, J = 1.5, 8.1 Hz), 6.84-6.88 (2H, m), 6.97 (1H, ddd, J = 1.5, 7.3, 8.1 Hz), 7.16 (1H, d, J = 7.3 Hz), 7.41 (2H, d, J = 8.1 Hz), 7.94 (2H, d, J = 8.1 Hz), 8.62 (1H, br.t, J = 5.9 Hz), 9.62 (1H, br.s).
IR (KBr) cm-1 = 3275, 1655, 1584, 1534, 1458, 1316, 747.

(0173)

Example 24.

N-(2-aminophenyl)-4-(N-(1-methyl-1 H-pyrrole-2-yl) carbonylamino methyl) benzamide (Table-1 = compound number 210).

Mp. 177-179 degrees (dec.).

1H NMR (270 MHz, DMSO-d6) delta ppm: 3.84 (3H, s), 4.46 (2H, d, J = 5.9 Hz), 4.88 (2H, br.s), 6.03 (1H, dd, J = 2.1, 4.4 Hz), 6.59 (1H, dd, J = 8.1, 8.1 Hz), 6.77 (1H, d, J = 8.1 Hz), 6.84-6.97 (2H, m), 7.16 (1H, d, J = 7.3 Hz), 7.41 (2H, d, J = 8.1 Hz), 7.93 (2H, d, J = 8.1 Hz), 8.61 (1H, t, J = 5.9 Hz), 9.62 (1H, br.s).

IR (KBr) cm-1 = 3325 (br.), 1630, 1551, 1520, 1507, 1324, 1265, 1154, 740.

(0174)

Example 25.

N-(2-aminophenyl)-4-(N-(isoxazole-5-yl) carbonylamino methyl) benzamide (Table-1 = compound number 212).

Mp. 183-185 deg C (dec.).

1H NMR (270 MHz, DMSO-d6) delta ppm: 4.53 (2H, d, J = 6.6 Hz), 4.89 (2H, br.s), 6.60 (1H, dd, J = 7.3, 7.3 Hz), 6.78 (1H, d, J = 7.3 Hz), 6.97 (1H, dd, J = 7.3, 8.1 Hz), 7.12 (1H, d, J = 2.1 Hz), 7.16 (1H, d, J = 8.1 Hz), 7.44 (2H, d, J = 8.1 Hz), 7.95 (2H, d, J = 8.1 Hz), 8.76 (1H, d, J = 1.5 Hz), 9.61 (1H, t, J = 5.9 Hz), 9.64 (1H, br.s).

IR (KBr) cm-1 = 3278 (br.), 1636, 1576, 1522, 1458, 1220, 749.

(0175)

Example 26.

N-(2-aminophenyl)-4-(N-(3-methyl iso thiazole-5-yl) carbonylamino methyl) benzamide (Table-1 = compound number 213).

Mp. 168-169 deg C.

1H NMR (270 MHz, DMSO-d6) delta ppm: 2.47 (3H, s), 4.54 (2H, d, J = 5.9 Hz), 4.89 (2H, br.s), 6.60 (1H, dd, J = 7.3, 7.3 Hz), 6.78 (1H, d, J = 7.3 Hz), 6.97 (1H, ddd, J = 1.0, 7.3, 8.1 Hz), 7.17 (1H, d, J = 7.3 Hz), 7.44 (2H, d, J = 8.1 Hz), 7.73 (1H, s), 7.96 (2H, d, J = 8.1 Hz), 9.44 (1H, t, J = 5.9 Hz), 9.64 (1H, br.s).

IR (KBr) cm-1 = 3310, 1637, 1503, 1294, 751.

(0176)

Example 27.

N-(2-aminophenyl)-4-(N-(imidazole-4-yl) carbonylamino methyl) benzamide (Table-1 = compound number 214).

Mp. (amorphous).

1H NMR (270 MHz, DMSO-d6) delta ppm: 4.49 (2H, d, J = 6.4 Hz), 4.87 (2H, br.s), 6.59 (1H, dd, J = 6.9, 6.9 Hz), 6.77 (1H, d, J = 6.9 Hz), 6.96 (1H, dd, J = 7.4, 7.4 Hz), 7.16 (1H, d, J = 6.9 Hz), 7.41 (2H, d, J = 6.9 Hz), 7.64 (1H, br.s), 7.73 (1H, br.s), 7.92 (2H, d, J = 6.9 Hz), 8.56 (1H, br.t, J = 6.4 Hz), 9.61 (1H, s), 12.5 (1H, br.s).

IR (KBr) cm-1 = 3278 (br.), 1636, 1576, 1522, 1458, 1220, 749.

(0177)

Example 28.

N-(2-aminophenyl)-4-(N-(3-aminophenyl) acetylamino methyl) benzamide (the compound of Table-1 = compound number 23).

Mp. 171-176 deg C.

1H NMR (270 MHz, DMSO-d6) delta ppm: 4.34 (2H, d, J = 5.9 Hz), 5.24 (4H, br.s), 6.48-6.63 (4H, m), 6.78-6.81 (1H, m), 6.94-7.00 (2H, m), 7.18 (1H, d, J = 8.1 Hz), 7.34 (2H, d, J = 8.1 Hz), 7.92 (2H, d, J = 8.1 Hz), 8.50 (1H, t, J = 5.9 Hz), 9.61 (1H, s).

(0178)

Example 2 9.

N-(2-aminophenyl)-4-(N-(pyridin-3-yl) acetylamino methyl) benzamide (Table-1 = compound number 74).

Mp. 127 deg C.

1H NMR (270 MHz, DMSO-d6) delta ppm: 3.84 (2H, s), 4.40 (2H, d, J = 5.8 Hz), 7.15-7.29 (3H, m), 7.37 (1H, d, J = 6.6 Hz), 7.43 (2H, d, J = 8.8 Hz), 7.96 (1H, m), 7.98 (2H, d, J = 8.8 Hz), 8.40 (1H, d, J = 8.8 Hz), 8.79-8.87 (3H, m), 10.20 (1H, s).

(0179)

Example 30.

N-(2-aminophenyl)-4-(N-(3-(pyridin-3-yl) propionyl) aminomethyl) benzamide (the compound of Table-1 = compound number 75).

Mp. 183-186 deg C.

1H NMR (270 MHz, DMSO-d6) delta ppm: 2.51 (2H, t, J = 7.3 Hz), 2.88 (2H, d, J = 7.3 Hz), 4.31 (2H, d, J = 5.9 Hz), 4.89 (2H, br.s), 6.60 (1H, dd, J = 7.3, 8.1 Hz), 6.78 (1H, d, J = 8.1 Hz), 6.97 (1H, ddd, J = 1.5, 7.3, 8.1 Hz), 7.16 (1H, d, J = 8.1 Hz), 7.23 (2H, d, J = 8.8 Hz), 7.28-7.33 (1H, m), 7.63 (1H, d, J = 8.1 Hz), 7.89 (2H, d, J = 8.1 Hz), 8.41-8.45 (3H, m), 9.62 (1H, br.s).

IR (KBr) cm-1 = 3407, 3313, 1640, 1552, 1522, 1456, 1309, 746, 717.

(0180)

Example 31.

N-(2-aminophenyl)-4-(N-(4-(pyridin-3-yl)-1,4-dioxobutyl) aminomethyl) benzamide (Table-1 = compound number 100).

Mp. 145-147 deg C (dec.).

1H NMR (270 MHz, DMSO-d6) delta ppm: 2.37-2.50 (2H, m), 2.62-2.68 (2H, m), 4.13 (2H, s), 4.86 (2H, s), 6.56-6.61 (1H, m), 6.76-6.79 (1H, m), 6.94-6.99 (1H, m), 7.10-7.39 (4H, m), 7.43-7.46 (1H, m), 7.78 (2H, d, J = 8.1 Hz), 8.60-8.64 (1H, m), 9.58 (1H, s).

IR (KBr) cm-1 = 3348, 1691, 1655, 1534, 1508, 1458, 1395, 1315, 1083, 746.

(0181)

Example 32.

N-(2-aminophenyl)-4-(N-(5-chloropyridin-3-yl) oxy acetylamino methyl) benzo amide (Table-1 = compound number 158).

Mp. 199-201 deg C.

1H NMR (270 MHz, DMSO-d6) delta ppm: 4.43 (2H, d, J = 6.6 Hz), 4.75 (2H, s), 4.87 (2H, br.s), 6.60 (1H, dd, J = 7.3, 8.1 Hz), 6.78 (1H, d, J = 8.1 Hz), 6.97 (1H, dd, J = 7.3, 8.1 Hz), 7.16 (1H, d, J = 8.1 Hz), 7.37 (2H, d, J = 8.1 Hz), 7.59 (1H, d, J = 2.2 Hz), 7.93 (2H, d, J = 8.1 Hz), 8.25 (1H, d, J = 1.5 Hz), 8.81 (1H, t, J = 6.6 Hz), 9.64 (1H, s).

IR (KBr) cm-1 = 3288, 3058, 1675, 1633, 1523, 1457, 1314, 912, 755.

(0182)
Example 33.
N-(2-amino-5-methoxyphenyl)-4-(N-(pyridin-3-yl) oxy acetylamino methyl) benzamide (Table-1 = compound number 175).

Mp. 141-144 deg C.
1H NMR (270 MHz, DMSO-d6) delta ppm: 3.66 (3H, s), 4.43 (2H, d, J = 5.9 Hz), 4.49 (2H, br.s), 4.68 (2H, s), 6.62 (1H, dd, J = 2.9, 8.8 Hz), 6.75 (1H, d, J = 8.8 Hz), 6.91 (1H, d, J = 2.2 Hz), 7.37 (4H, m), 7.92 (2H, d, J = 8.8 Hz), 8.21 (1H, dd, J = 1.5, 4.4 Hz), 8.35 (1H, d, J = 2.7 Hz), 8.81 (1H, s), 9.65 (1H, s).

(0183)
Example 34.
N-(2-aminophenyl)-4-(N-(3-(pyridin-3-yl)-1,3-dioxo propyl) aminomethyl) benzamide (Table-1 = compound number 98).

Mp. 204-206 deg C .1 HNMR (270 MHz, DMSO-d 6) delta ppm: 4.08 (4/3H, s), 4.39 (4/3H, d, J = 5.9 Hz), 4.49 (2/3H, d, J = 5.9 Hz), 4.90 (2H, br.s), 5.93 (1/3H, s), 6.60 (1H, t, J = 7.3 Hz), 6.78 (1H, d, J = 8.1 Hz), 6.97 (1H, t, J = 7.3 Hz), 7.16 (1H, d, J = 7.3 Hz), 7.3-7.7 (3H, m), 7.8-8.4 (3H, m), 8.6-9.2 (3H, m), 9.64 (1H, s), 14.74 (1/3H, s).
IR (KBr) cm-1 = 3282, 1690, 1645, 1527, 1421, 1314, 1217, 1028, 994, 911, 753, 701.

(0184)
Example 35.
N-(2-aminophenyl)-4-(N-(N-(pyridin-3-yl) aminoacetyl) aminomethyl) benzamide (Table-1 = compound number 96).

Mp. (amorphous).
1H NMR (270 MHz, DMSO-d6) delta ppm: 3.77 (2H, d, = 6.6 Hz), 4.37 (2H, d, J = 5.9 Hz), 4.87 (2H, br.s), 6.27 (1H, t, J = 5.9 Hz), 6.60 (1H, dd, J = 7.3, 7.3 Hz), 6.78 (1H, d, 7.3 Hz), 6.87 (1H, d, J = 8.1 Hz), 6.96 (1H, dd, J = 7.3, 8.1 Hz), 7.09 (1H, d, J = 4.4 Hz), 7.12 (1H, d, J = 4.4 Hz),

7.16 (1H, d, J = 8.1 Hz), 7.33 (2H, d, J = 8.8 Hz), 7.81 (1H, d, J = 4.4 Hz), 7.91 (2H, d, J = 7.3 Hz), 7.99 (1H, d, J = 2.9 Hz), 8.59 (1H, br.t, J = 5.1 Hz), 9.63 (1H, br.s).
IR (KBr) cm-1 = 3350, 1658, 1525, 1502, 1314, 750.

(0185)
Example 36.
N-(2-aminophenyl)-4-(N-(2-aminothiazole-4-yl) acetylamino methyl) benzamide (Table-1 = compound number 220).

Mp. (amorphous).
1H NMR (270 MHz, DMSO-d6) delta ppm: 3.34 (2H, s), 4.35 (2H, d, J = 5.9 Hz), 4.87 (2H, s), 6.25 (1H, s), 6.59 (1H, dd, J = 7.3, 7.3 Hz), 6.78 (1H, d, J = 7.3 Hz), 6.87 (2H, s), 6.96 (1H, dd, J = 7.3, 7.3 Hz), 7.16 (1H, d, J = 7.3 Hz), 7.37 (2H, d, J = 8.1 Hz), 7.93 (2H, d, J = 8.1 Hz), 8.44 (1H, t, J = 5.9 Hz), 9.62 (1H, s).

(0186)
Example 37.
N-(2-aminophenyl)-4-(N-(quinolin-6-yl) carbonylamino methyl) benzamide (Table-1 = compound number 231).

Mp. 209-210 deg C.
1H NMR (270 MHz, DMSO-d6) delta ppm: 4.62 (2H, d, J = 5.9 Hz), 4.88 (2H, s), 6.60 (1H, t, J = 7.7 Hz), 6.78 (1H, d, J = 7.3 Hz), 6.95 (1H, d, J = 7.3 Hz), 7.17 (1H, d, J = 7.3 Hz), 7.49 (2H, d, J = 8.8 Hz), 7.62 (1H, dd, J = 4.4, 8.1 Hz), 7.96 (2H, d, J = 8.8 Hz), 8.10 (1H, d, J = 8.8 Hz), 8.23 (1H, dd, J = 2.2, 8.8 Hz), 8.38 (1H, m), 8.49 (1H, d, J = 8.1 Hz), 8.58 (1H, s), 8.99 (1H, s), 9.64 (1H, s).
IR (KBr) cm-1 = 3301, 1640, 1614, 1545, 1496, 1312, 910, 853, 745.

(0187)
Example 38.
N-(2-aminophenyl)-4-(N-(furo (3,2-b) pyridin-2-yl) carbonylamino methyl) benzamide (Table-1 = compound number 233).

Mp. 191 deg C (dec.).
1H NMR (270 MHz, DMSO-d6) delta ppm: 4.58 (2H, d, J = 5.9 Hz), 4.88 (2H, s), 6.57-6.62 (1H, m), 6.76-6.79 (1H, m), 6.93-6.99 (1H, m), 7.15-7.25 (1H, m), 7.45-7.52 (3H, m), 7.74 (1H, s), 7.95 (2H, d, J = 8.1 Hz), 8.13 (1H, d, J = 8.8 Hz), 8.63 (1H, d, J = 3.7 Hz), 9.54 (1H, t, J = 5.9 Hz), 9.64 (1H, s).
IR (KBr) cm-1 = 3406, 1662, 1529, 1507, 1420, 1313, 1209, 1139, 1170, 1139, 924, 741.

(0188)
Example 39.
N-(2-aminophenyl)-4-(N-(furo (2,3-c) pyridin-2-yl) carbonylamino methyl) benzamide (Table-1 = compound number 234).

Mp. 210 deg C (dec.).
1H NMR (270 MHz, DMSO-d6) delta ppm: 4.58 (2H, J = 6.6 Hz), 4.87 (2H, s), 6.57-6.62 (1H, m), 6.76-6.79 (1H, m), 6.93-6.99 (1H, m), 7.14-7.17 (1H, m), 7.47 (2H, d, J = 8.1 Hz), 7.66 (1H, s), 7.82 (1H, d, J = 4.4 Hz), 7.96 (2H, d, J = 8.1 Hz), 8.48 (1H, d, J = 5.1 Hz), 9.06 (1H, s), 9.60-9.64 (2H, m).
IR (KBr) cm-1 = 3320, 1653, 1632, 1598, 1457, 1424, 1308, 1187, 1033, 853, 749.

(0189)
Example 40.
N-(2-hydroxyphenyl)-4-(N-(3-(pyridin-3-yl) propionyl) aminomethyl) benzamide (Table-1 = compound number 125).

Mp. (amorphous).
1H NMR (270 MHz, CD3OD) delta ppm: 2.61 (2H, t, J = 7.3 Hz), 3.00 (2H, t, J = 7.3 Hz), 4.39 (2H, s), 7.04 (1H, ddd, J = 1.5, 8.1, 8.1 Hz), 7.25 (2H, d, J = 8.1 Hz), 7.33 (1H, dd, J = 5.1, 8.1 Hz), 7.69 (1H, d, J = 8.1 Hz), 7.85 (2H, d, J = 8.1 Hz), 7.86 (1H, d, J = 8.1 Hz), 8.41 (2H, br.s).
IR (neat) cm-1 = 3276, 1645, 1614, 1536, 1509, 1435, 1415, 1385, 1333, 1280, 1247, 1091, 737.

(0190)
Example 41.

N-(2-hydroxyphenyl)-4-(N-(pyridin-3-yl) oxy acetylamino methyl) benzamide (Table-1 = compound number 93).

Mp. (amorphous).
1H-NMR (270 MHz, DMSO-d6) = 4.43 (2H, d, J = 6.6 Hz), 4.69 (2H, s), 6.83 (1H, t, J = 6.6 Hz), 6.91 (1H, d, J = 8.1 Hz), 7.68 (1H, d, J = 6.6 Hz), 7.82 (2H, d, J = 8.1 Hz), 8.21 (1H, d, J = 4.4 Hz), 8.35 (1H, d, J = 2.2 Hz), 8.81 (1H, t, J = 6.6 Hz), 9.48 (1H, s), 9.75 (1H, s).
IR (KBr) cm-1 = 3399,1664,1535,1236,1064.

(0191)
Example 42.
N-(2-hydroxyphenyl)-4-(N-(pyridin-3-yl) acetylamino methyl) benzamide (Table-1 = compound number 117).

Mp. 201-202 deg C.
1H NMR (270 MHz, DMSO-d6) delta ppm: 3.56 (2H, s), 4.37 (2H, d, J = 5.9 Hz), 6.83 (1H, ddd, J = 1.5, 8.1, 8.1 Hz), 6.92 (1H, br.d, J = 8.1 Hz), 7.03 (1H, ddd, J = 1.5, 8.1, 8.1 Hz), 7.34 (1H, dd, J = 3.7, 8.1 Hz), 7.37 (2H, d, J = 8.1 Hz), 7.70 (2H, d, J = 8.1 Hz), 7.91 (2H, d, J = 8.1 Hz), 8.45 (1H, br.d, J = 3.7 Hz), 8.49 (1H, s), 8.73 (1H, t, J = 5.9 Hz), 9.47 (1H, s), 9.73 (1H, br.s).
IR (KBr) cm-1 = 3272, 3067, 1661, 1647, 1598, 1536, 1455, 1334, 1288, 1194, 1024, 742.

(0192)
Example 43.
N-(2-aminophenyl)-4-(N-(pyridin-3-yl) oxy acetyl-N-(3-(pyridin-3-yl) propyl) aminomethyl) benzamide (Table-1 = compound number 91).

Mp. (amorphous).
1H NMR (270 MHz, DMSO-d6) delta ppm: 1.77-1.93 (2H, m), 2.50-2.63 (2H, m), 3.16-3.30 (2H, m), 4.63 (1.2H, s), 4.71 (0.8H, s), 4.88 (1.2H, s), 4.95 (0.8H, s), 5.05 (2H, s), 6.57-6.63 (1H, m), 6.77-6.79 (1H, m), 6.94-7.00 (1H, m), 7.11-7.42 (5H, m), 7.58-7.64 (1H, m), 7.92-8.02 (2H, m), 8.15-8.43 (5H, m), 9.65 (0.6H, s), 9.69 (0.4H, s). (mixture of rotational isomer).

(0193)

Example 44.

N-(2-aminophenyl)-4-(N-methyl-N-(pyridin-3-yl) oxy acetyl) aminomethyl benzamide (Table-1 = compound number 92).

Mp. 117-120 deg C.

1H NMR (270 MHz, DMSO-d6) delta ppm: 2.84 and 2.99 (total 3H, s), 4.60 and 4.69 (total 2H, s), 4.90 (2H, br.s), 4.99 and 5.08 (total 2H, s), 6.60 (1H, dd, J = 7.3, 8.1 Hz), 6.78 (1H, d, J = 8.1 Hz), 6.97 (1H, dd, J = 7.3, 7.3 Hz), 7.16 (1H, d, J = 7.3 Hz), 7.30-7.43 (4H, m), 7.95 and 8.01 (total 2H, d, J = 8.1 Hz), 8.17 (1H, d, J = 4.4 Hz), 8.31 (1H, d, J = 2.9 Hz), 9.65 and 9.68 (total 1H, br.s). (mixture of rotational isomer).

IR (KBr) cm-1 = 3298, 1665, 1501, 1425, 1310, 1276, 1254, 1078, 799, 746, 703.

(0194)

Example 45.

Synthesis of N-(2-aminophenyl)-4-(N-(pyridin-3-yl) oxamoyl aminomethyl) benzamide (Table-1 = compound number 95).

(45-1) .

N-(pyridin-3-yl) oxamic acid ethyl ester 388 mg (2 mmol) and compound 638 mg (2 mmol) of step (1-4) of Example 1 were dissolved in ethanol, and it was heated with stirring in 40-50 degrees for two hours 30 minutes. The precipitated crystals were recovered by filtration and were washed with ethanol 2 ml and ethyl ether 3 ml. The obtained crystals were dried, and N-(2-(N-tert-butoxycarbonyl) aminophenyl)-4-(N-(pyridin-3-yl) oxamoyl aminomethyl) benzamide 724 mg (yield 74 %) were obtained.

1H NMR (270 MHz, DMSO-d6) delta ppm: 1.44 (9H, s), 4.49 (2H, d, J = 5.9 Hz), 7.10-7.30 (2H, m), 7.35-7.57 (5H, m), 7.93 (2H, d, J = 8.1 Hz), 8.21 (1H, br.d, J = 5.1 Hz), 8.35 (1H, dd, J = 1.5, 5.1 Hz), 8.68 (1H, br.s), 9.00 (1H, d, J = 2.9 Hz), 9.70 (1H, t, J = 5.9 Hz), 9.82 (1H, s), 10.98 (1H, br.s).

(0195)

(45-2) .

Compound 720 mg of step (45-1) was suspended in methanol 8 ml, and 4 N hydrochloric acid-dioxane solution 8 ml was added. The mixture was stirred for three hours, and made alkaline by

introducing in to dilute sodium hydroxide aqueous solution, thereafter precipitated crystals were recovered. The obtained crystals were recrystallised with THF / methanol = 1/1, and target substance 280 mg were obtained.

Mp. 254-258 deg C (dec.).
1H NMR (270 MHz, DMSO-d6) delta ppm: 4.67 (2H, d, J = 5.9 Hz), 4.89 (2H, br.s), 6.59 (1H, dd, J = 7.3 Hz), 6.77 (1H, d, J = 8.1 Hz), 6.97 (1H, dd, J = 6.6, 7.3 Hz), 7.16 (1H, d, J = 8.1 Hz), 7.38-7.44 (1H, m), 7.43 (2H, d, J = 8.1 Hz), 7.95 (2H, d, J = 8.1 Hz), 8.18-8.24 (1H, m), 8.34 (1H, dd, J = 1.5, 4.4 Hz), 9.00 (1H, d, J = 2.1 Hz), 9.63 (1H, s), 9.69 (1H, br.t, J = 6.6 Hz), 10.97 (1H, br.s).
IR (KBr, cm-1) = 3312, 3270, 1663, 1636, 1521, 1312, 1296, 1019.

(0196)
Example 46.
Synthesis of N-(2-aminophenyl)-4-(N-(pyridin-3-yl) oxy acetylamino methyl) benzamide (Table-1 = compound number 61).

(46-1).
DMF (2 ml) solution of 3-hydroxypyridine 0.48 g (5.0 mmol) was added dropwise to DMF (2 ml) suspension of sodium hydride (60 % oil form suspension) 0.22 g (5.5 mmol) at room temperature, thereafter the mixture was stirred for one hour. Obtained brown solution was cooled with ice and next, bromoacetic acid tert-butyl ester 0.81 ml (5.5 mmol) were added, and the mixture was stirred under ice cooling for one hour and was stirred at room temperature for two hours. Water was added and thereafter was extracted with ethyl acetate. Organic layer was washed with saturated aqueous sodium chloride solution, and thereafter it was dried, and the residue obtained by elimination of the solvent by distillation was refined by silica gel column chromatography (chloroform:ethyl acetate = 5:1), thereby 3-pyridyl oxyacetate tert-butyl ester 0.34 g (yield 32.5 %) were obtained as a colourless oily substance.

1H NMR (270 MHz, CDCl3) delta ppm: 1.49 (9H, s), 4.56 (2H, s), 7.18-7.24 (2H, m), 8.26 (1H, dd, J = 1.5, 3.6 Hz), 8.32 (1H, d, J = 2.9 Hz).

(0197)

(46-2) .

Trifluoroacetic acid 2 ml were added to dichloromethane (2 ml) solution of compound 0.14 g (0.67 mmol) of step (46-1) and the mixture was stirred at room temperature for three hours. The solvent was eliminated by distillation, and next, diisopropyl ether is added, and the precipitated solid was recovered by filtration, and by drying, 3-pyridyl oxyacetate trifluoroacetate 0. 15 g (yield 83.8 %) were obtained as the straw-coloured solid.

1H NMR (270 MHz, DMSO-d6) delta ppm: 4.86 (2H, s), 7.57 (1H, dd, J = 4.4, 8.1 Hz), 7.67 (1H, ddd, J = 1.5, 1.5, 8.8 Hz), 8.31 (1H, d, J = 5.1 Hz), 8.46 (1H, d, J = 2.1 Hz), 13.00 (1H, br.s).

(0198)

(46-3) .

Triethylamine 0.14 ml (1.0 mmol) were added to dichloromethane (5 ml) suspension of compound 100 mg (0.37 mmol) of step (46-2) and compound 255 mg (0.75 mmol) of step (1-4) of Example 1, and it was cooled with ice. Dichloromethane (6 ml) solution of 2-chloro-1,3-dimethyl imidazolinium chloride 140 mg (0.83 mmol) was added under ice cooling, and stirring was stirred for seven hours while being warmed to room temperature, and next, it was left to stand at room temperature overnight. Water and saturated aqueous sodium chloride solution were added, thereafter it was extracted with chloroform.

(0199)

The organic layer was washed with saturated aqueous sodium chloride solution, and thereafter it was dried, and the residue obtained by elimination of the solvent by distillation was refined by silica gel column chromatography (ethyl acetate:methanol = 10:1), thereby N-(2-(N-tert-butoxycarbonyl) aminophenyl)-4-(N-(pyridin-3-yl) oxy acetylamino methyl) benzamide 0.37 g (quantitative) were obtained as a colourless oily substance.

Mp. 154-155 deg C.

1H NMR (270 MHz, CDCl3) delta ppm: 1.52 (9H, s), 4.62 (2H, s), 4.63 (2H, d, J = 7.3 Hz), 6.76 (1H, br.s), 6.90-7.00 (1H, br.s), 7.15-7.35 (5H, m), 7.40 (2H, d, J = 8.1 Hz), 7.82 (1H, d, J = 8.1 Hz), 7.95 (2H, d, J = 8.1 Hz), 8.32 (1H, dd, J = 2.1, 4.4 Hz), 8.37 (1H, d, J = 2.8 Hz), 9.20 (1H, br.s).

(0200)

(46-4) .

4 N hydrochloric acid-dioxane (2 ml) was added to dioxane (2 ml)-methanol (2 ml) solution of compound 175 mg (0.37 mmol) of step (46-3), and the mixture was stirred at room temperature for two hours. Saturated aqueous sodium bicarbonate was added and thereafter it was extracted with ethyl acetate. Organic layer was washed with saturated aqueous sodium chloride solution, and thereafter it was dried, and methanol and diisopropyl ether were added in the residue obtained by elimination of the solvent by distillation, and the precipitated solid was recovered by filtration, and N-(2-aminophenyl)-4-(N-(pyridin-3-yl) oxy acetylamino methyl) benzamide 90 mg (yield 64.6 %) were obtained as the opal solid by drying.

1H NMR (270 MHz, DMSO-d6) delta ppm: 4.42 (2H, d, J = 5.9 Hz), 4.69 (2H, s), 4.89 (2H, br.s), 6.59 (1H, dd, J = 7.3, 8.1 Hz), 6.78 (1H, d, J = 8.1 Hz), 6.97 (1H, dd, J = 6.6, 7.3 Hz), 7.16 (1H, d, J = 7.3 Hz), 7.33-7.39 (4H, m), 7.92 (2H, d, J = 8.1 Hz), 8.21 (1H, dd, J = 1.5, 4.4 Hz), 8.35 (1H, d, J = 2.9 Hz), 8.80 (1H, br.t, J = 5.9 Hz), 9.63 (1H, br.s).
IR (KBr) cm-1 = 3307, 1672, 1631, 1523, 1456, 1429, 1269, 1231, 803, 756.

(0201)

Example 47.

Synthesis of N-(2-aminophenyl)-4-(N-(2-(pyridin-3-yl) oxy) propionyl aminomethyl) benzamide (Table-4 = compound number 3).

(0202)

(47-1) .

Dried DMF (10 ml) solution of 3-hydroxypyridine 2.85 g (30 mmol) was added dropwise to dried DMF (10 ml) suspension of sodium hydride (60 % oil form suspending) 1.20 g (30.0 mmol) at room temperature so as to become 40 degrees or less and next, the mixture was stirred at room temperature for 90 minutes. Dried DMF (10 ml) solution of 2-bromopropionic acid tert-butyl ester 6.28 g (30 mmol) was gradually added dropwise while maintaining an internal temperature at 5-10 degrees under ice cooling and the mixture was stirred for four hours and next, it was warmed to room temperature. It was neutralised by the addition of saturated aqueous sodium bicarbonate and next was extracted with ethyl acetate. Organic layer was washed with water, saturated aqueous sodium chloride solution, and thereafter it was dried, and the residue obtained by

elimination by distillation of the solvent was refined by silica gel column chromatography (N-hexane:ethyl acetate = 2:1), thereby 2-(pyridin-3-yl) oxy propionic acid tert-butyl ester 4.15 g (yield 62 %) were obtained as brown oily substance.

1H-NMR (270 MHz, CDCl3) delta ppm: 1.44 (9H, s), 1.61 (3H, d, J = 7.3 Hz), 4.66 (1H, q, J = 7.3 Hz), 7.13-7.23 (2H, m) 8.24 (1H, dd, J = 1.5, 4.4 Hz), 8.29 (1H, d, J = 2.1 Hz).

(0203)

(47-2) .

Trifluoroacetic acid (9 ml) was added to dichloromethane (9 ml) solution of compound 1.65 g (7.4 mmol) obtained with step (47-1) while being held at 30 degrees or less and thereafter the mixture was stirred at room temperature for eight hours. The solvent was eliminated by distillation, and next, diisopropyl ether was added, and the precipitated solid was recovered by filtration, and 2-(pyridin-3-yl) oxy propionic acid trifluoroacetate 1.86 g (yield 43.5 %) were obtained as the pale-brown solid by drying.

1H-NMR (270 MHz, DMSO-d6) delta ppm: 1.53 (3H, d, J = 6.6 Hz), 5.12 (1H, q, J = 6.6 Hz), 7.60-7.75 (2H, m), 8.35 (1H, d, J = 5.1 Hz), 8.47 (1H, s), 12.9 (1H, br.s).

(0204)

(47-3) .

Compound 1.02 g (3.0 mmol) that were obtained with step (1-4) of Example 1 and the compound 0.98 g (3.5 mmol) obtained with step (47-2) were suspended in dichloromethane (20 ml), and next triethylamine 1.3 ml (9.0 mmol) were added, and it was cooled with ice. Dichloromethane (5 ml) solution of 2-chloro-1,3-dimethyl imidazolinium chloride 0.59 g (3.5 mmol) was dropwise added under ice cooling and next, furthermore was stirred for two hours. Saturated aqueous sodium bicarbonate was added and neutralisation caused and next was extracted with chloroform. Organic layer was washed with saturated aqueous sodium chloride solution, and thereafter it was dried, and the residue from which the solvent was eliminated by distillation was refined by silica gel column chromatography (ethyl acetate:methanol = 10:1), thereby N-(2-(N-tert-butoxycarbonyl amino) phenyl)-4-(N-(2-(pyridin-3-yl) oxy propionyl) aminomethyl) benzamide 1.64 g were obtained as mixture of 1,3-dimethyl-2-imidazolinone by refining.

1H-NMR (270 MHz, CDCl3) delta ppm: 1.51 (9H, s), 1.64 (3H, d, J = 7.3 Hz), 4.54 (2H, m), 4.78 (1H, q, J = 6.6 Hz), 6.87 (2H, br.s), 7.13-7.30 (6H, m), 7.81 (1H, d, J = 7.3 Hz), 7.90 (2H, d, J = 8.1 Hz), 8.29 (1H, dd, J = 1.5, 4.4 Hz), 8.33 (1H, d, J = 2.1 Hz), 9.22 (1H, br.s).

(0205)

(47-4) .

Compound 1.64 g obtained with step (47-3) were dissolved in dioxane (10 ml)-methanol (4 ml). 4 N hydrochloric acid-dioxane solution (10 ml) was added at room temperature and the mixture was stirred for two hours. Saturated aqueous sodium bicarbonate was added and neutralisation caused and next it was extracted with ethyl acetate. Organic layer was washed with saturated aqueous sodium chloride solution, and next and was dried, and methanol and diisopropyl ether were added to the solvent residue from which the solvent was elliminated by distillation, and the precipitated solid was recovered by filtration, and by drying, N-(2-aminophenyl)-4-(N-(2-(pyridin-3-yl) oxy) propionyl aminomethyl) benzamide 0. 71 g (yield 60.5 %) were obtained as white solid.

(0206)

Mp. 171-173 deg C (dec.).

1H-NMR (270 MHz, DMSO-d6) delta ppm: 1.51 (3H, d, J = 6.6 Hz), 4.36 (2H, d, J = 5.9 Hz), 4.89 (2H, br.s), 4.90 (1H, t, J = 6.6 Hz), 6.60 (1H, dd, J = 6.6, 7.3 Hz), 6.78 (1H, d, J = 8.1 Hz), 6.97 (1H, dd, J = 6.6, 7.3 Hz), 7.15 (1H, d, J = 7.3 Hz), 7.27 (2H, d, J = 8.1 Hz), 7.33-7.37 (2H, m), 7.89 (2H, d, J = 8.1 Hz), 8.21 (1H, dd, J = 2.9, 2.9 Hz), 8.32 (1H, d, J = 1.5 Hz), 8.82 (1H, t, J = 5.9 Hz), 9.63 (1H, br.s).

(0207)

Example 48.

Synthesis of N-(2-aminophenyl)-4-(N-(pyridin-3-yl) methoxycarbonylamino methyl) benzamide (Table-1 = compound number 82).

(48-1) .

3-pyridinomethanol 384 mg (3.52 mmol) were dissolved in dried THF of 5 ml, and N,N-carbonyldiimidazole 523 mg (3.22 mmol) were added at room temperature. The mixture was stirred

for one hour, and next dried THF solution 6 ml of compound 1.0 g (2.93 mmol) of step (1-4) of Example 1 were added.

(0208)
It was left overnight to stand at room temperature, and thereafter chloroform 100 ml were added, and it was washed three times with water 20 ml. Thereafter, it was washed with saturated aqueous sodium chloride solution and thereafter was dried with anhydrous magnesium sulphate. The solvent was eliminated by distillation under reduced pressure and was refined by silica gel column chromatography (chloroform:methanol = 30:1), and N-(2-(N-tert-butoxycarbonyl) aminophenyl)-4-(N-(pyridin-3-yl) methoxycarbonylamino methyl) benzamide 1.27 g were obtained as the amorphous state solid (quantitative).

1H NMR (270 MHz, CDCl3) delta ppm: 1.51 (9H, s), 4.45 (2H, d, J = 5.9 Hz), 5.16 (1H, s), 7.10-7.50 (7H, m), 7.70 (1H, d, J = 8.1 Hz), 7.80 (1H, d, J = 7.3 Hz), 7.93 (1H, d, J = 8.1 Hz), 8.57 (1H, d, J = 4.4 Hz), 8.63 (1H, s), 9.17 (1H, s).

(0209)
(48-2) .
Compound 1.2 g (2.8 mmol) of step (48-1) were dissolved in methanol 10 ml. 4 N hydrochloric acid-dioxane solution 20 ml were added and the mixture was stirred at room temperature for one hour 30 minutes. It was poured in to dilute sodium hydroxide aqueous solution, and next, it was extracted three times with chloroform 60 ml. It was washed twice with saturated aqueous sodium chloride solution, and next it was dried with anhydrous magnesium sulphate, and it was concentrated, and the crystals of 0.88 g were obtained. Thereafter, it was recrystallised from ethanol 16 ml, and N-(2-aminophenyl)-4-(N-(pyridin-3-yl) methoxycarbonylamino methyl) benzamide 668 mg (yield 73 %) were obtained.

(0210)
Mp. 159-160 deg C.
1H NMR (270 MHz, DMSO-d6) delta ppm: 4.28 (2H, d, J = 5.9 Hz), 4.86 (2H, s), 5.10 (2H, s), 6.60 (1H, t, J = 7.3 Hz), 6.78 (1H, d, J = 7 Hz), 6.97 (1H, t, J = 7 Hz), 7.17 (1H, d, J = 8 Hz), 7.30-7.50 (3H, m), 7.78 (1H, d, J = 8 Hz), 7.93 (2H, d, J = 8 Hz), 8.53 (1H, d, J = 3.7 Hz), 8.59 (1H, s), 9.61 (1H, s).

IR (KBr) cm-1 = 3295, 1648, 1541, 1508, 1457, 1309, 1183, 742.

By process same as in Example 48, the compounds of Example 49 to Example 87 were synthesised. Below melting point (mp.) of the compound, 1H NMR, measured value of IR are shown.

(0211)
Example 49.
N-(2-aminophenyl)-4-(N-(benzyloxycarbonyl) aminomethyl) benzamide (Table-1 = compound number 11).

Mp. 174-178 deg C.
1H NMR (270 MHz, DMSO-d6) delta ppm: 4.28 (2H, d, J = 5.9 Hz), 4.89 (2H, br.s), 5.06 (2H, s), 6.59 (1H, dd, J = 7.3, 8.1 Hz), 6.78 (1H, d, J = 8.1 Hz), 6.97 (1H, dd, J = 7.3, 8.1 Hz), 7.16 (1H, d, J = 7.3 Hz), 7.30-7.40 (6H, m), 7.93 (3H, m), 9.63 (1H, s).
IR (KBr) cm-1 = 3332, 1687, 1652, 1536, 1456, 1279, 747.

(0212)
Example 50.
N-(2-aminophenyl)-4-(N-(4-(imidazole-1-yl) benzyl) oxycarbonyl aminomethyl) benzamide (Table-1 = compound number 47).

Mp. 195-198 deg C.
1H NMR (270 MHz, DMSO-d6) delta ppm: 4.29 (2H, d, J = 6.6 Hz), 4.88 (2H, s), 5.10 (2H, s), 6.60-6.63 (1H, m), 6.78 (1H, d, J = 8.1 Hz), 6.97 (1H, t, J = 7.3 Hz), 7.11 (1H, s), 7.16 (1H, d, J = 7.3 Hz), 7.37 (2H, d, J = 8.1 Hz), 7.49 (2H, d, J = 8.8 Hz), 7.66 (2H, d, J = 8.1 Hz), 7.74 (1H, s), 7.92-7.96 (3H, m), 8.25 (1H, s), 9.62 (1H, s).

(0213)
Example 51.
N-(2-aminophenyl)-4-(N-(pyridin-2-yl) methoxycarbonylamino methyl) benzamide (Table-1 = compound number 171).

Mp. 166-167 deg C.
1H NMR (270 MHz, DMSO-d6) delta ppm: 4.30 (2H, d, J = 5.9 Hz), 4.88 (2H, br.s), 5.12 (2H, s), 6.60 (1H, dd, J = 7.3, 8.1 Hz), 6.78 (1H, d, J = 8.1 Hz), 6.97 (1H, ddd, J = 1.5, 7.3, 8.1 Hz), 7.16 (1H, d, J = 7.3 Hz), 7.33 (1H, dd, J = 3.7, 7.3 Hz), 7.40 (3H, d, J = 8.1 Hz), 7.83 (1H, ddd, J = 1.5, 7.3, 8.1 Hz), 7.94 (2H, d, J = 8.1 Hz), 8.03 (1H, t, J = 5.9 Hz), 8.55 (1H, d, J = 5.1 Hz), 9.62 (1H, br.s).
IR (KBr) cm-1 = 3334, 1694, 1632, 1580, 1276, 755.

(0214)
Example 52.
N-(2-aminophenyl)-4-(N-(2-(pyridin-2-yl) ethoxycarbonyl) aminomethyl) benzamide (Table-1 = compound number 172).
Mp. 146-148 deg C.
1H NMR (270 MHz, DMSO-d6) delta ppm: 3.04 (2H, t, J = 6.6 Hz), 4.23 (2H, d, J = 5.9 Hz), 4.36 (2H, t, J = 6.6 Hz), 4.88 (2H, br.s), 6.60 (1H, dd, J = 7.3, 8.1 Hz), 6.78 (1H, d, J = 8.1 Hz), 6.97 (1H, dd, J = 7.3, 8.1 Hz), 7.15-7.30 (3H, m), 7.34 (2H, d, J = 8.1 Hz), 7.69-7.77 (2H, m), 7.92 (2H, d, J = 7.3 Hz), 8.50 (1H, d, J = 4.4 Hz), 9.62 (1H, br.s).
IR (KBr) cm-1 = 3330, 1690, 1633, 1594, 1524, 1277, 760.

(0215)
Example 53.
N-(2-aminophenyl)-4-(N-(6-methylpyridin-2-yl) methoxycarbonylamino methyl) benzamide (Table-1 = compound number 179).

Mp. 138 deg C.
1H NMR (270 MHz, DMSO-d6) delta ppm: 2.47 (3H, s), 4.30 (2H, d, J = 5.9 Hz), 5.07 (4H, s), 6.63 (1H, t, J = 8.1 Hz), 6.80 (1H, d, J = 7.34), 6.98 (1H, t, J = 8.1 Hz), 7.18 (3H, d, J = 7.3 Hz), 7.40 (2H, d, J = 8.1 Hz), 7.71 (1H, t, J = 8.1 Hz), 7.94 (2H, d, J = 8.1 Hz), 8.03 (1H, t, J = 5.9 Hz), 9.66 (1H, s).
IR (KBr) cm-1 = 3335, 1693, 1634, 1259.

(0216)
Example 54.

N-(2-aminophenyl)-4-(N-(2-(pyridin-3-yl) ethoxycarbonyl) aminomethyl) benzamide (Table-1 = compound number 83).

Mp. 120-125 deg C.
1H NMR (270 MHz, DMSO-d6) delta ppm: 2.91 (2H, t, J = 6.6 Hz), 4.22 (4H, t, J = 6.6 Hz), 4.89 (2H, s), 6.55-6.63 (1H, m), 6.78 (1H, dd, J = 8.1, 1.5 Hz), 6.97 (1H, t, J = 6.6 Hz), 7.17 (1H, d, J = 6.6 Hz), 7.33 (3H, d, J = 8.1 Hz), 7.69 (1H, d, J = 8.1 Hz), 7.79 (1H, t, J = 6.6 Hz), 7.93 (2H, d, J = 8.0 Hz), 8.43-8.49 (2H, m), 9.62 (1H, s).
IR (KBr) cm-1 = 3234, 1705, 1655, 1260.

(0217)
Example 55.
N-(2-aminophenyl)-4-(N-(3-(pyridin-3-yl) propyl oxycarbonyl) aminomethyl) benzamide (Table-1 = compound number 84).

Mp. 121-124 deg C.
1H NMR (270 MHz, DMSO-d6) delta ppm: 1.83-1.94 (2H, m), 2.67 (2H, t, J = 7.3 Hz), 3.98 (2H, t, J = 6.6 Hz), 4.26 (2H, d, J = 5.9 Hz), 4.89 (2H, br.s), 6.60 (1H, dd, J = 8.1, 8.1 Hz), 6.78 (1H, d, J = 7.3 Hz), 6.97 (1H, ddd, J = 1.5, 7.3, 8.1 Hz), 7.16 (1H, d, J = 8.1 Hz), 7.29-7.33 (1H, m), 7.37 (1H, d, J = 8.1 Hz), 7.64 (1H, d, J = 8.1 Hz), 7.81 (1H, dd, J = 5.9, 6.6 Hz), 7.94 (2H, d, J = 8.1 Hz), 8.40-8.44 (2H, m), 9.63 (1H, br.s).
IR (KBr) cm-1 = 3348, 1696, 1635, 1523, 1458, 1302, 1272, 1141, 1019, 754, 713.

(0218)
Example 56.
N-(2-aminophenyl)-4-(N-(2-methylpyridin-3-yl) methoxycarbonylamino methyl) benzamide (Table-1 = compound number 142).

Mp. 164-165 deg C.
1H NMR (270 MHz, DMSO-d6) delta ppm: 2.49 (3H, s), 4.28 (2H, d, J = 6.6 Hz), 4.89 (2H, s), 5.10 (2H, s), 6.60 (1H, t, J = 6.6 Hz), 6.78 (1H, d, J = 8.1 Hz), 6.90 (1H, t, J = 7.3 Hz), 7.17 (1H, d, J = 7.3 Hz), 7.21-7.26 (1H, m), 7.37 (2H, d, J = 8.1 Hz), 7.68 (1H, d, J = 6.6 Hz), 7.92-8.00 (3H, m), 8.39 (1H, d, J = 4.4 Hz), 9.62 (1H, s).

IR (KBr) cm-1 = 3332, 1719, 1630, 1260.

(0219)

Example 57.

N-(2-aminophenyl)-4-(N-(6-methylpyridin-3-yl) methoxycarbonylamino methyl) benzamide (Table-1 = compound number 144).

Mp. 164-165 deg C.

1H NMR (270 MHz, DMSO-d6) delta ppm: 2.46 (3H, s), 4.27 (2H, d, J = 6.6 Hz), 4.88 (2H, s), 5.05 (2H, s), 6.59 (1H, dt, J = 1.5, 8.1 Hz), 6.78 (1H, dd, J = 8.1, 1.5 Hz), 6.97 (1H, dt, J = 1.5, 7.3 Hz), 7.17 (1H, d, J = 7.3 Hz), 7.26 (1H d, J = 8.1 Hz), 7.36 (2H, d, J = 8.1 Hz), 7.67 (1H, dd, J = 8.1, 2.2 Hz), 7.93 (3H, d, J = 8.1 Hz), 8.45 (1H, d, J = 1.5 Hz), 9.62 (1H, s).

IR (KBr) cm-1 = 3293, 1701, 1632, 1260.

(0220)

Example 58.

N-(2-aminophenyl)-4-(N-(2-chloropyridin-3-yl) methoxycarbonylamino methyl) benzamide (Table-1 = compound number 155).

Mp. (amorphous).

1H NMR (270 MHz, DMSO-d6) delta ppm: 4.30 (2H, d, J = 5.9 Hz), 5.00 (2H, s), 5.13 (2H, s), 6.61 (1H, t, J = 7.3 Hz), 6.79 (1H, dd, J = 8.1, 1.5 Hz), 6.98 (1H, dt, J = 1.5, 7.3 Hz), 7.17 (1H, d, J = 6.6 Hz), 7.39 (2H, d, J = 8.8 Hz), 7.47-7.52 (1H, m), 7.91-7.96 (3H, m), 8.08 (1H, t, J = 5.9 Hz), 8.40 (1H, dd, J = 4.4, 1.5 Hz), 9.64 (1H, s).

IR (KBr) cm-1 = 3340, 1702, 1632, 1273.

(0221)

Example 59.

N-(2-aminophenyl)-4-(N-(6-chloropyridin-3-yl) methoxycarbonylamino methyl) benzamide (Table-1 = compound number 157).

Mp. 180-185 deg C.

1H NMR (270 MHz, DMSO-d6) delta ppm: 4.24 (2H, d, J = 5.9 Hz), 4.89 (2H, br.s), 5.10 (2H, s), 6.60 (1H, t, J = 7.3 Hz), 6.78 (1H, d, J = 8.1 Hz), 6.97 (1H, dt, J = 1.5, 8.1 Hz), 7.16 (1H, d, J = 6.6 Hz), 7.37 (2H, d, J = 8.1 Hz), 7.56 (1H, d, J = 8.1 Hz), 7.85-8.02 (4H, m), 8.44 (1H, d, J = 2.2 Hz), 9.62 (1H, s).
IR (KBr) cm-1 = 3346,3282, 1696, 1533, 1271.

(0222)
Example 60.
N-(2-aminophenyl)-4-(N-(pyridin-4-yl) methoxycarbonylamino methyl) benzamide (Table-1 = compound number 181).

Mp. 180-183 deg C.
1H NMR (270 MHz, DMSO-d6) delta ppm: 4.30 (2H, d, J = 6.6 Hz), 4.89 (2H, s), 5.12 (2H, s), 6.60 (1H, dd, J = 7.3, 7.3 Hz), 6.78 (1H, dd, J = 1.5, 7.3 Hz), 6.97 (1H, ddd, J = 1.5, 7.3, 8.1 Hz), 7.16 (1H, d, J = 7.3 Hz), 7.34 (2H, d, J = 5.9 Hz), 7.39 (2H, d, J = 8.1 Hz), 7.94 (2H, d, J = 8.1 Hz), 8.09 (1H, t, J = 5.9 Hz), 8.57 (1H, d), 9.64 (1H, br.s).
IR (KBr) cm-1 = 3394,3290, 1711, 1645, 1624, 1535, 1504, 1321, 1251, 1138, 1049,763.

(0223)
Example 61.
N-(2-aminophenyl)-4-(N-(2-(thiophen-3-yl) ethoxycarbonyl) aminomethyl) benzamide (Table-1 = compound number 203).

Mp. (amorphous).
1H NMR (270 MHz, DMSO-d6) delta ppm: 2.90 (2H, t, J = 7.3 Hz), 4.17-4.26 (4H, m), 4.89 (2H, s), 6.60 (1H, t, J = 8.1 Hz), 6.78 (1H, d, J = 6.6 Hz), 6.97 (1H, t, J = 7.3 Hz), 7.06 (1H, d, J = 5.1 Hz), 7.17 (1H, d, J = 7.3 Hz), 7.26 (1H, s), 7.36 (2H, d, J = 8.1 Hz), 7.47 (1H, t, J = 2.2 Hz), 7.81 (1H, t, J = 5.9 Hz), 7.93 (2H, d, J = 8.1 Hz), 9.63 (1H, s).
IR (KBr) cm-1 = 3314, 1716, 1638, 1252.

(0224)
Example 62.

N-(2-aminophenyl)-4-(N-(3-phenyloxazol-5-yl) methoxycarbonylamino methyl) benzamide (Table-1 = compound number 211).

Mp. 192-195 deg C.
1H NMR (270 MHz, DMSO-d6) delta ppm: 4.30 (2H, d, J = 5.9 Hz), 4.89 (2H, s), 5.25 (2H, s), 6.60 (1H, t, J = 6.6 Hz), 6.68 (1H, d, J = 8.1 Hz), 6.94 (1H, t, J = 7.3 Hz), 7.09 (1H, s), 7.16 (1H, d, J = 7.3 Hz), 7.39 (2H, d, J = 8.1 Hz), 7.51 (4H, d, J = 2.2 Hz), 7.87-7.96 (5H, m), 8.12 (1H, t, J = 5.9 Hz), 9.63 (1H, s).
IR (KBr) cm-1 = 3292, 1718, 1630, 1262.

(0225)
Example 63.
N-(2-aminophenyl)-4-(N-(thiazole-5-yl) methoxycarbonylamino methyl) benzamide (Table-1 = compound number 216).

Mp. (amorphous).
1H NMR (270 MHz, DMSO-d6) delta ppm: 4.28 (2H, d, J = 5.9 Hz), 4.91 (2H, br.s), 5.30 (2H, s), 6.60 (1H, dd, J = 7.3, 7.3 Hz), 6.78 (1H, d, J = 8.1 Hz), 6.97 (1H, dd, J = 7.3, 8.1 Hz), 7.16 (1H, d, J = 7.3 Hz), 7.36 (2H, d, J = 8.1 Hz), 7.91-8.00 (4H, m), 9.09 (1H, s), 9.63 (1H, s).
IR (KBr) cm-1 = 3346 (br.), 1697, 1636, 1525, 1456, 1271, 873, 753.

(0226)
Example 64.
N-(2-aminophenyl)-4-(N-(2-(4-methylthiazol-5-yl) ethoxycarbonyl) aminomethyl) benzamide (Table-1 = compound number 217).

Mp. 130-133 deg C.
1H NMR (270 MHz, DMSO-d6) delta ppm: 2.32 (3H, s), 3.07 (2H, t, J = 5.9 Hz), 4.15 (2H, t, J = 5.9 Hz), 4.25 (2H, d, J = 6.6 Hz), 4.89 (2H, s), 6.60 (1H, t, J = 5.9 Hz), 6.78 (1H, dd, J = 7.3, 1.5 Hz), 6.97 (1H, dt, J = 1.5, 7.3 Hz), 7.16 (1H, d, J = 8.1 Hz), 7.35 (2H, d, J = 8.1 Hz), 7.83 (1H, t, J = 5.9 Hz), 7.94 (2H, d, J = 8.1 Hz), 8.85 (1H, s), 9.62 (1H, s).
IR (KBr) cm-1 = 3350, 1691, 1635, 1270.

(0227)

Example 65.

N-(2-aminophenyl)-4-(N-(1-methylpiperidin-3-yl) methoxycarbonylamino methyl) benzamide (Table-1 = compound number 225).

Mp. 130-135 deg C.

1H NMR (270 MHz, DMSO-d6) delta ppm: 1.49-1.78 (3H, m), 1.83-2.01 (3H, m), 2.30 (3H, s), 2.85 (2H, s), 3.74-3.94 (2H, m), 4.25 (2H, d, J = 5.8 Hz), 6.55-6.62 (3H, m), 6.78 (1H, d, J = 8.1 Hz), 6.97 (1H, t, J = 7.3 Hz), 7.16 (1H, d, J = 8.1 Hz), 7.37 (2H, d, J = 8.1 Hz), 7.79 (1H, t, J = 6.6 Hz), 7.93 (2H, d, J = 8.0 Hz), 9.66 (1H, s).

IR (KBr) cm-1 = 3323, 2722, 1702, 1648, 1263.

(0228)

Example 66.

N-(2-aminophenyl)-4-(N-(4-methylpiperazin-1-yl) methoxycarbonylamino methyl) benzamide (Table-1 = compound number 227).

Mp. (amorphous).

1H NMR (270 MHz, DMSO-d6) delta ppm: 1.73 (2H, t, J = 6.6 Hz), 2.36-2.63 (13H, m), 4.00 (2H, t, J = 6.6 Hz), 4.30 (2H, d, J = 5.8 Hz), 6.55-6.63 (4H, m), 6.78 (1H, d, J = 6.6 Hz), 6.97 (1H, t, J = 7.3 Hz), 7.16 (1H, d, J = 7.3 Hz), 7.37 (2H, d, J = 8.7 Hz), 7.73 (1H, t, J = 5.9 Hz), 7.94 (2H, d, J = 8.0 Hz), 9.66 (1H, s).

IR (KBr) cm-1 = 3341, 2706, 1701, 1262.

(0229)

Example 67.

N-(2-aminophenyl)-4-(N-(tetrahydrofuran-3-yl) methoxycarbonylamino methyl) benzamide (Table-1 = compound number 221).

Mp. (amorphous).

1H NMR (270 MHz, DMSO-d6) delta ppm: 1.50-1.60 (1H, m), 1.88-2.00 (1H, m), 2.44-2.54 (1H, m), 3.41-3.47 (1H, m), 3.56-3.77 (3H, m), 3.85-4.04 (2H, m), 4.25 (2H, d, J = 5.9 Hz), 4.89 (2H, s), 6.60 (1H, dd, J = 7.3, 7.3 Hz), 6.78 (1H, d, J = 8.1 Hz), 6.97 (1H, dd, J = 7.3, 8.1 Hz), 7.17

(1H, d, J = 8.1 Hz), 7.37 (2H, d, J = 8.1 Hz), 7.81 (1H, t, J = 5.9 Hz), 7.94 (2H, d, J = 8.1 Hz), 9.62 (1H, br.s).
IR (KBr) cm-1 = 3349, 1695, 1635, 1523, 1457, 1259, 754.

(0230)
Example 68.
N-(2-aminophenyl)-4-(N-(phenoxy carbonyl) aminomethyl) benzamide (Table-1 = compound number 12).

Mp. 174-175 deg C.
1H NMR (270 MHz, DMSO-d6) delta ppm: 4.36 (2H, d, J = 5.9 Hz), 4.90 (2H, br.s), 6.60 (1H, dd, J = 7.3, 7.3 Hz), 6.77 (1H, dd, J = 7.3, 7.3 Hz), 6.98 (1H, ddd, J = 1.5, 7.3, 7.3 Hz), 7.05-7.24 (4H, m), 7.39-7.46 (4H, m), 7.97 (2H, d, J = 8.1 Hz), 8.41 (1H, t, J = 5.9 Hz), 9.65 (1H, br.s).
IR (KBr) cm-1 = 3443, 3362, 3313, 1732, 1706, 1636, 1527, 1493, 1458, 1305, 1217, 748.

(0231)
Example 69.
N-(2-aminophenyl)-4-(N-(pyridin-3-yl) oxycarbonyl aminomethyl) benzamide (Table-1 = compound number 81).

Mp. 209 deg C (dec.).
1H NMR (270 MHz, DMSO-d6) delta ppm: 4.38 (2H, d, J = 6.6 Hz), 4.90 (2H, br.s), 6.55-6.63 (1H, m), 6.78 (1H, d, J = 8.1 Hz), 7.00 (1H, dd, J = 7.3, 7.3 Hz), 7.17 (1H, d, J = 8.8 Hz), 7.37-7.47 (3H, m), 7.64 (1H, d, J = 8.8 Hz), 7.97 (2H, d, J = 8.1 Hz), 8.43 (2H, d, J = 3.1 Hz), 8.59 (1H, t, J = 5.9 Hz), 9.66 (1H, br.s).

(0232)
Example 70.
N-(2-amino-5-fluorophenyl)-4-(N-(pyridin-3-yl) methoxycarbonylamino methyl) benzamide (Table-1 = compound number 110).

Mp. 160-162 deg C.

1H NMR (270 MHz, DMSO-d6) delta ppm: 4.28 (2H, d, J = 6.6 Hz), 4.81 (2H, s), 5.10 (2H, s), 6.70-6.90 (2H, m), 7.10-8.00 (8H, m), 8.53 (1H, d, J = 3.6 Hz), 8.59 (1H, s), 9.61 (1H, s).
IR (KBr) cm-1 = 3269, 1716, 1638, 1488, 1436, 1247, 1141, 1043, 744.

(0233)
Example 71.
N-(2-aminophenyl)-4-(N-(2-aminophenyl) methoxycarbonylamino methyl) benzamide (Table-1 = compound number 51).

Mp. 149-151 deg C (dec.).
1H NMR (270 MHz, DMSO-d6) delta ppm: 4.28 (2H, d, J = 5.9 Hz), 4.88 (2H, s), 4.96 (2H, s), 5.06 (2H, s), 6.53 (1H, dd, J = 7.3, 7.3 Hz), 6.56-6.67 (2H, m), 6.78 (1H, dd, J = 1.5, 8.1 Hz), 6.93-7.12 (3H, m), 7.16 (1H, d, J = 6.6 Hz), 7.38 (2H, d, J = 8.1 Hz), 7.86 (1H, t-like, J = 5.9 Hz), 7.93 (2H, d, J = 8.1 Hz), 9.61 (1H, s).
IR (KBr) cm-1 = 3336, 1685, 1632, 1527, 1276, 748.

(0234)
Example 72.
N-(2-aminophenyl)-4-(N-(quinuclidin-3-yl) oxycarbonyl aminomethyl) benzamide (Table-1 = compound number 228).

Mp. (amorphous).
1H NMR (270 MHz, DMSO-d6) delta ppm: 1.30-1.90 (4H, m), 1.90 (1H, br.s), 2.45-2.80 (6H, m), 3.04-3.13 (1H, m), 4.15 (2H, d, J = 5.9 Hz), 4.55-4.60 (1H, m), 4.88 (2H, br.s), 6.60 (1H, ddd, J = 1.5, 7.3, 7.3 Hz), 6.78 (1H, d, J = 8.1 Hz), 6.97 (1H, ddd, J = 1.5, 7.3, 7.3 Hz), 7.17 (1H, d, J = 6.6 Hz), 7.37 (2H, d, J = 8.1 Hz), 7.78 (1H, t, J = 5.9 Hz), 7.94 (1H, d, J = 7.3 Hz), 9.62 (1H, s).
IR (KBr) cm-1 = 3328, 2942, 1700, 1648, 1504, 1259, 749.

(0235)
Example 73.
N-(2-aminophenyl)-4-(N-(3-aminophenyl) methoxycarbonylamino methyl) benzamide (Table-1 = compound number 52).

Mp. 149-153 deg C (dec.).
1H NMR (270 MHz, DMSO-d6) delta ppm: 4.27 (2H, d, J = 5.9 Hz), 4.88 and 4.89 (total 4H, each br.s), 5.08 (2H, s), 6.47-6.63 (3H, m), 6.78 (1H, d, J = 8.1 Hz), 6.94-7.02 (2H, m), 7.15 (1H, dd, J = 7.3, 8.8 Hz), 7.37 (2H, d, J = 8.1 Hz), 7.84 (1H, t, J = 5.9 Hz), 7.93 (2H, d, J = 8.8 Hz), 9.61 (1H, br.s).
IR (KBr) cm-1 = 3367, 1682, 1632, 1523, 1457, 1261, 754.

(0236)
Example 74.
N-(2-aminophenyl)-4-(N-(1-methyl imidazole-5-yl) methoxycarbonylamino methyl) benzamide (Table-1 = compound number 218).

Mp. 162-165 deg C (dec.).
1H NMR (270 MHz, DMSO-d6) delta ppm: 3.62 (3H, s), 4.27 (2H, d, J = 5.9 Hz), 4.91 (2H, br.s), 5.05 (2H, s), 6.60 (1H, dd, J = 7.3, 7.3 Hz), 6.78 (1H, d, J = 8.1 Hz), 6.95-7.00 (2H, m), 7.16 (1H, d, J = 7.3 Hz), 7.36 (2H, d, J = 8.1 Hz), 7.63 (1H, s), 7.87-7.95 (3H, m), 9.64 (1H, br.s).
IR (KBr) cm-1 = 3293, 1688, 1651, 1534, 1506, 1259, 1121, 1043, 748.

(0237)
Example 75.
N-(2-amino-4-chlorophenyl)-4-(N-(pyridin-3-yl) methoxycarbonylamino methyl) benzamide (Table-1 = compound number 113).

Mp. 167-170 deg C.
1H NMR (270 MHz, DMSO-d6) delta ppm: 4.28 (2H, d, J = 5.9 Hz), 5.10 (2H, s), 5.21 (2H, s), 6.72 (1H, dd, J = 2.2, 8.1 Hz), 6.81 (1H, d, J = 2.2 Hz), 7.16 (1H, d, J = 8.1 Hz), 7.37 (2H, d, J = 8.1 Hz), 7.78 (1H, d, J = 8.1 Hz), 7.92 (2H, d, J = 8.1 Hz), 8.53 (1H, d, J = 4.4 Hz), 8.59 (1H, s), 9.60 (1H, s).
IR (KBr) cm-1 = 3347, 3062, 2931, 1653, 1576, 1505, 1456, 1428, 1301, 1232, 1114, 1070, 1019.

(0238)
Example 76.

N-(2-aminophenyl)-4-(N-(5-methoxypyridin-3-yl) methoxycarbonylamino methyl) benzamide (Table-1 = compound number 161).

Mp. 169-170 deg C.
1H NMR (270 MHz, DMSO-d6) delta ppm: 3.83 (3H, s), 4.29 (2H, d, J = 6.6 Hz), 4.87 (2H, s), 5.09 (2H, s), 6.57-6.62 (1H, m), 6.76-6.79 (1H, m), 6.94-6.99 (1H, m), 7.14-7.18 (1H, m), 7.36-7.39 (3H, m), 7.91-7.99 (3H, m), 8.19-8.30 (2H, m), 9.63 (1H, s).
IR (KBr) cm-1 = 3330, 1694, 1633, 1524, 1457, 1298, 1269, 1045, 760.

(0239)
Example 77.
N-(2-aminophenyl)-4-(N-(pyrazin-2-yl) methoxycarbonylamino methyl) benzamide (Table-1 = compound number 192).

Mp. 182 deg C.
1H NMR (270 MHz, DMSO-d6) delta ppm: 4.30 (2H, d, J = 6.6 Hz), 4.88 (2H, br.s), 5.20 (2H, s), 6.60 (1H, dd, J = 7.3, 8.1 Hz), 6.78 (1H, d, J = 8.1 Hz), 6.97 (1H, dd, J = 6.6, 8.1 Hz), 7.16 (1H, d, J = 7.3 Hz), 7.39 (2H, d, J = 8.8 Hz), 7.94 (2H, d, J = 8.8 Hz), 8.08 (1H, t-like, J = 6.6 Hz), 8.61 (1H, s), 8.65 (1H, s), 8.68 (1H, s), 9.63 (1H, s).
IR (KBr) cm-1 = 3266, 1709, 1632, 1535, 1508, 1284, 1055, 1022, 744.

(0240)
Example 78.
N-(2-amino-5-methoxyphenyl)-4-(N-(pyridin-3-yl) methoxycarbonylamino methyl) benzamide (Table-1 = compound number 121).

Mp. 141-143 deg C.
1H NMR (270 MHz, DMSO-d6) delta ppm: 3.66 (3H, s), 4.29 (2H, d, J = 5.9 Hz), 4.51 (2H, br.s), 5.10 (2H, s), 6.63 (1H, dd, J = 2.9, 8.8 Hz), 6.74 (1H, d, J = 8.8 Hz), 6.91 (1H, d, J = 2.2 Hz), 7.38 (2H, d, J = 8.8 Hz), 7.41 (1H, s), 7.79 (1H, d, J = 8.1 Hz), 7.92 (2H, d, J = 8.1 Hz), 7.98 (1H, t, J = 5.9 Hz), 8.54 (1H, d, J = 3.7 Hz), 8.60 (1H, s), 9.65 (1H, s).

(0241)

Example 79.
N-(2-aminophenyl)-4-(N-(pyridine 3-yl) methyl-N-(pyridin-3-yl) methoxycarbonylamino methyl) benzamide (Table-1 = compound number 109).

Mp. (amorphous).
1H NMR (270 MHz, DMSO-d6) delta ppm: 4.50 (2H, s), 4.56 (2H, s), 4.87 (2H, s), 5.21 (2H, s), 6.60 (1H, t, J = 7.7 Hz), 6.78 (1H, d, J = 7.3 Hz), 6.97 (1H, d, J = 7.3 Hz), 7.17 (1H, d, J = 7.3 Hz), 7.20-7.50 (4H, m), 7.60-8.00 (4H, m), 8.40-8.60 (4H, m), 9.65 (1H, s).
IR (KBr) cm-1 = 3268, 1700, 1504, 1246, 1120, 940, 714.

(0242)
Example 80.
N-(2-aminophenyl)-4-(N-(3-(pyridin-3-yl) propyl)-N-(pyridin-3-yl) methoxycarbonylamino methyl) benzamide (Table-1 = compound number 120).

Mp. (amorphous).
1H NMR (270 MHz, DMSO-d6) delta ppm: 1.75-1.90 (2H, m), 2.48-2.62 (2H, m), 3.20-3.36 (2H, m), 4.55 (2H, s), 4.89 (2H, s), 5.16 (2H, s), 6.57-6.63 (1H, m), 6.76-6.80 (1H, m), 6.94-6.99 (1H, m), 7.14-7.17 (1H, m), 7.32-7.74 (6H, m), 7.94 (2H, d, J = 8.1 Hz), 8.30-8.65 (4H, m), 9.64 (1H, s).

(0243)
Example 81.
N-(2-hydroxyphenyl)-4-(N-(pyridin-3-yl) methyl-N-(pyridin-3-yl) methoxycarbonylamino methyl) benzamide (Table-1 = compound number 115).

Mp. (amorphous).
1H NMR (270 MHz, DMSO-d6) = 4.52 (2H, s), 4.57 (2H, s), 5.20 (2H, s), 6.84 (1H, t, J = 6.6 Hz), 6.93 (1H, d, J = 6.6 Hz), 7.03 (1H, d, J = 7.3 Hz), 7.37 (4H, m), 7.68 (2H, dd, J = 1.5, 8.1 Hz), 7.92 (2H, br.s), 8.53 (4H, m), 9.49 (1H, s), 9.77 (1H, br.s).
IR (KBr) cm-1 = 3035, 1698, 1243, 1118, 754, 640.

(0244)

Example 82.

N-(2-hydroxyphenyl)-4-(N-(pyridin-3-yl) methoxycarbonylamino methyl) benzamide (Table-1 = compound number 111).

Mp. 162-164 deg C.

1H NMR (270 MHz, DMSO-d6) = 4.29 (1H, d, J = 5.9 Hz), 5.10 (2H, s), 6.83 (1H, t, J = 8.1 Hz), 6.92 (1H, d, J = 6.6 Hz), 7.07 (1H, t, J = 6.6 Hz), 7.39 (2H, d, J = 8.8 Hz), 7.43 (1H, d, J = 5.1 Hz), 7.68 (2H, d, J = 8.1 Hz), 7.80 (1H, d, J = 8.1 Hz), 7.92 (2H, d, J = 8.1 Hz), 7.99 (1H, t, J = 5.9 Hz), 8.54 (1H, d, J = 4.4 Hz), 8.60 (1H, s), 9.49 (1H, s), 9.76 (1H, br.s).

IR (KBr) cm-1 = 3333, 3259, 1694, 1645, 1529, 1267, 720.

(0245)

Example 83.

N-(2,4-dihydroxyphenyl)-4-(N-(pyridin-3-yl) methoxycarbonylamino methyl) benzamide (Table-1 = compound number 116).

Mp. (amorphous).

1H NMR (270 MHz, DMSO-d6) = 4.27 (2H, d, J = 6.6 Hz), 5.10 (2H, s), 6.20 (2H, dd, J = 2.2, 8.1 Hz), 6.39 (2H, d, J = 2.9 Hz), 6.88 (2H, d, J = 8.8 Hz), 7.33 (1H, d, J = 8.1 Hz), 7.41 (1H, dd, J = 5.1, 7.1 Hz), 7.89 (1H, d, J = 8.8 Hz), 7.98 (1H, t, J = 6.6 Hz), 8.05 (2H, s), 8.52 (1H, m), 8.59 (1H, s), 9.30 (2H, br.s).

IR (KBr) cm-1 = 3387, 1702, 1612, 1311, 1169, 845.

(0246)

Example 84.

N-(2-hydroxy-5-methylphenyl)-4-(N-(pyridin-3-yl) methoxycarbonylamino methyl) benzamide (Table-1 = compound number 118).

Mp. 155-155.5 deg C.

1H NMR (270 MHz, DMSO-d6) = 2.22 (3H, s), 4.29 (2H, d, J = 5.8 Hz), 5.11 (2H, s), 6.82 (2H, m), 7.39 (2H, d, J = 8.8 Hz), 7.42 (2H, m), 7.51 (1H, s), 7.79 (1H, d, J = 8.1 Hz), 7.92 (1H, d, J = 8.1 Hz), 7.98 (1H, t, J = 5.9 Hz), 8.54 (1H, d, J = 4.4 Hz), 8.60 (1H, s), 9.48 (2H, d, J = 8.1 Hz).

IR (KBr) cm-1 = 3306, 1723, 1655, 1525, 801, 639.

(0247)

Example 85.

N-(2-hydroxy-5-methoxyphenyl)-4-(N-(pyridin-3-yl) methoxycarbonylamino methyl) benzamide (Table-1 = compound number 119).

Mp. 175-176 deg C.

1H NMR (270 MHz, DMSO-d6) = 3.69 (3H, s), 4.29 (2H, d, J = 5.9 Hz), 5.10 (2H, s), 6.63 (1H, dd, J = 2.9, 8.7 Hz), 6.84 (1H, d, J = 8.8 Hz), 7.41 (4H, m), 7.79 (1H, d, J = 8.1 Hz), 7.91 (1H, d, J = 8.1 Hz), 7.99 (1H, t, J = 5.9 Hz), 8.54 (1H, d, J = 5.1 Hz), 8.60 (1H, s), 9.31 (1H, s), 9.45 (1H, s).

IR (KBr) cm-1 = 3305, 1687, 1573, 1262, 1039, 868.

(0248)

Example 86.

N-(2-aminophenyl)-4-(N-(2-(pyridin-3-yl) ethoxycarbonyl) amino) benzamide (Table-1 = compound number 124).

Mp. (amorphous).

1H NMR (270 MHz, DMSO-d6) delta ppm: 3.00 (2H, t, J = 6.6H), 4.37 (2H, t, J = 6.6 Hz), 4.87 (2H, br.s), 6.60 (1H, t, J = 7.3 Hz), 6.97 (1H, t, J = 7.3 Hz), 7.15 (1H, d, J = 7.3 Hz), 7.36 (1H, dd, J = 4.4, 8.1 Hz), 7.56 (2H, d, J = 8.8 Hz), 7.92 (2H, d, J = 8.8 Hz), 8.46 (1H, d, J = 4.4 Hz), 8.54 (1H, d, J = 2.2 Hz), 9.95 (1H, s).

IR (KBr) cm-1 = 3285, 1695, 1519, 1315, 1233, 1079.

(0249)

Example 87.

N-(2-aminophenyl)-5-((pyridin-3-yl) methoxycarbonyl) aminobenzo furan-2-carboxamido (Table-3 = compound number 2).

Mp. 173-174 deg C.

1H NMR (270 MHz, DMSO-d6) delta ppm: 5.22 (2H, s), 6.60 (1H, dd, J = 8.1, 8.1 Hz), 6.79 (1H, dd, J = 1.5, 8.1 Hz), 7.00 (1H, dd, J = 8.1, 8.1 Hz), 7.20 (1H, dd, J = 1.5, 8.1 Hz), 7.44 (1H, m), 7.48 (1H, dd, J = 1.5, 8.8 Hz), 7.61 (1H, d, J = 8.8 Hz), 7.67 (1H, s), 7.88 (1H, dd, J = 1.5, 8.1

Hz), 7.96 (1H, d, J = 1.5 Hz), 8.56 (1H, dd, J = 1.5, 4.8 Hz), 8.68 (1H, d, J = 1.5 Hz), 9.83 (1H, s), 9.91 (1H, s).
IR (KBr) cm-1 = 3308, 1707, 1667, 1584, 1536, 1452, 1316, 1248, 1157, 1128, 1070, 955, 879, 795, 748, 710.

(0250)
Example 88.
Synthesis of N-(2-aminophenyl)-4-(N-(pyridin-3-yl) methoxy thiocarbonyl aminomethyl) benzamide (Table-1 = compound number 88)

(88-1) 3-pyridinemethanol 20 mg (0.18 mmol) were dissolved in dried THF of 5 ml, and N,N-thiocarbonyl di imidazole 30 mg (0.16 mmol) were added at room temperature. The mixture was stirred overnight, and next compound 50 mg (0.14 mmol) of step of Example 1 (1-4) were added.

(0251)
It was left overnight to stand at room temperature, and thereafter chloroform 100 ml were added, and it was washed three times by water 20 ml. Thereafter, it was washed with saturated aqueous sodium chloride solution and thereafter was dried with anhydrous magnesium sulphate. The solvent was eliminated by distillation under reduced pressure and was refined by silica gel column chromatography (chloroform:methanol = 30:1), and N-(2-(N-tert butoxycarbonyl) aminophenyl)-4-(N-(pyridin-3-yl) methoxy thiocarbonyl aminomethyl) benzamide 70 mg (yield 88 %) were obtained as amorphous.

1H NMR (270 MHz, DMSO-d6) delta ppm: 1.45 (9H, s), 4.73 (2H, d, J = 5.9 Hz), 5.52 (2H, s), 6.73-7.33 (3H, m), 7.35-7.43 (2H, m), 7.58-7.95 (5H, m), 8.14-8.65 (3H, m), 9.80 (1H, s), 9.91 (1H, br.t).

(0252)
(88-2) .
Compound 50 mg (0.10 mmol) of step (88-1) were dissolved in methanol 3 ml. 4 N hydrochloric acid-dioxane solution 3 ml were added and the mixture was stirred at room temperature for one hour 30 minutes. It was poured into dilute sodium hydroxide aqueous solution, and hydrochloric acid was neutralised, and next it was extracted three times by chloroform 10 ml. It was washed

twice with saturated aqueous sodium chloride solution, and next it was dried with anhydrous magnesium sulphate, and it was concentrated, and N-(2-aminophenyl)-4-(N-(pyridin-3-yl) methoxy thiocarbonyl aminomethyl) benzamide of 34 mg (yield 87 %) was obtained.

Mp. 154-156 deg C (dec.).
1H NMR (270 MHz, DMSO-d6) delta ppm: 4.73 (2H, d, J = 5.9 Hz), 4.88 (2H, s), 5.52 (2H, s), 6.60 (1H, t, J = 7.3 Hz), 6.77 (1H, d, J = 8.1 Hz), 6.96 (1H, t, J = 8.1 Hz), 7.16 (1H, d, J = 7.3 Hz), 7.29-7.41 (3H, m), 7.83-7.95 (3H, m), 8.50-8.56 (1H, m), 8.65 (1H, s), 9.62 (1H, s), 9.93 (1H, s).
IR (KBr) cm-1 = 3204, 3035, 1631, 1523, 1456, 1289, 1191, 920, 753.

(0253)
Example 89.
Synthesis of N-(2-aminophenyl)-4-(N'-(pyridin-3-yl methyl) ureide methyl) benzamide (Table-1 = compound number 88).

(89-1) .
N,N'-carbonyldiimidazole 0.42 g (2.4 mmol) were added at room temperature into THF (10 ml) solution of 3-picoryl amine 0.28 g (2.6 mmol), and the mixture was stirred for one hour. Compound 0.58 g (1.8 mmol) of step (1-4) of Example 1 were added at room temperature and were stirred for three hours, and next, it was left to stand into this solution overnight.

(0254)
Water was added, and it was diluted, and next, it was extracted with ethyl acetate. Organic layer was washed with saturated aqueous sodium chloride solution, and next it was dried, and the residue obtained by the elimination of the solvent by distillation was purified by silica gel column chromatography (ethyl acetate-methanol = 10:1), and N-(2-(N-tert-butoxycarbonyl) amino) phenyl-4-(N'-(pyridin-3-yl methyl) ureide methyl) benzamide 0.77 g (yield 90 %) were obtained as the white amorphous state solid.

1H NMR (270 MHz, CDCl3) delta ppm: 1.46 (9H, s), 4.20 (2H, d, J = 5.1 Hz), 4.28 (2H, d, J = 4.3 Hz), 6.10-6.30 (2H, m), 7.00-7.25 (4H, m), 7.33 (1H, d, J = 7.3 Hz), 7.49-7.54 (2H, m), 7.58-7.64 (3H, m), 7.75 (1H, s), 8.28 (1H, br.s), 8.39 (1H, d, J = 5.1 Hz), 9.65 (1H, br.s).

(0255)

(89-2) .

4 N hydrochloric acid-dioxane (4 ml) was added to dioxane (4 ml)-methanol (2 ml) solution of compound 0.63 g (1.32 mmol) obtained with step (89-1) and the mixture was stirred at room temperature two hours. Saturated aqueous sodium bicarbonate was added and thereafter was extracted with ethyl acetate-methyl ethyl ketone. Organic layer was washed with saturated aqueous sodium chloride solution, and thereafter it was dried, and N-(2-aminophenyl)-4-(N'-(pyridin-3-yl methyl) ureide methyl) benzamide 0.37 g (yield 74.7 %) were obtained as the brown solid by washing the residue obtained by elimination of the solvent by distillation with diisopropyl ether.

(0256)

Mp. (amorphous) .1H NMR (270 MHz, DMSO-d6) delta ppm: 4.27 (2H, d, J = 5.9 Hz), 4.31 (2H, d, J = 5.9 Hz), 4.89 (2H, br.s), 6.57-6.63 (3H, m), 6.78 (1H, d, J = 8.1 Hz), 6.97 (1H, dd, J = 7.3, 8.1 Hz), 7.17 (1H, d, J = 7.3 Hz), 7.32-7.38 (3H, m), 7.66 (1H, d, J = 8.1 Hz), 7.93 (2H, d, J = 8.1 Hz), 8.44 (1H, d, J = 5.1 Hz), 8.49 (1H, d, J = 2.1 Hz), 9.63 (1H, br.s).

IR (KBr) cm-1 = 3344, 3241, 1645, 1560, 1527, 1505, 1283, 751, 708.

(0257)

By process same as in Example 89, the compounds of Example 90 to Example 95 were synthesised. Below melting point (mp.) of the compound, 1H NMR, measured value of IR are shown.

(0258)

Example 90.

N-(2-aminophenyl)-4-(N'-(3-aminophenyl) ureide methyl) benzamide (Table-1 = compound number 24).

Mp. 206-208 deg C (dec.).

1H NMR (270 MHz, DMSO-d6) delta ppm: 4.35 (2H, d, J = 5.9 Hz), 4.93 (4H, br.s), 6.13 (1H, d, J = 7.3 Hz), 6.51-6.62 (3H, m), 6.74-6.98 (3H, m), 7.12-7.18 (1H, m), 7.41 (2H, d, J = 8.1 Hz), 7.94 (2H, d, J = 8.1 Hz), 8.28 (1H, s), 9.61 (1H, s).

IR (KBr) cm-1 = 3356,3269, 1640, 1555, 1495, 1458, 1308, 1236,753.

(0259)
Example 91.
N-(2-aminophenyl)-4-(N'-(pyridin-3-yl) ureide methyl) benzamide (Table-1 = compound number 87).

Mp. 187-190 deg C.
1H NMR (270 MHz, DMSO-d6) delta ppm: 4.39 (2H, d, J = 5.9 Hz), 4.89 (2H, br.s), 6.59 (1H, d, J = 7.3, 7.3 Hz), 6.77 (1H, d, J = 6.6 Hz), 6.88 (1H, t, J = 5.9 Hz), 6.97 (1H, ddd, J = 1.5, 6.6, 7.3 Hz), 7.16 (1H, d, J = 8.1 Hz), 7.26 (1H, dd, J = 4.4, 8.1 Hz), 7.42 (2H, d, J = 8.8 Hz), 7.95 (2H, d, J = 8.1 Hz), 7.89-7.96 (1H, m), 8.12 (1H, dd, J = 1.5, 4.4 Hz), 8.56 (1H, d, J = 3.0 Hz), 8.85 (1H, s), 9.62 (1H, s).
IR (KBr) cm-1 = 3248, 1663, 1541, 1423, 1280, 1054.

(0260)
Example 92.
N-(2-aminophenyl)-4-(N'-(3-aminophenyl) thioureide methyl) benzamide (Table-1 = compound number 25).

Mp. 123 deg C (dec.).
1H NMR (270 MHz, DMSO-d6) delta ppm: 4.80 (2H, d, J = 5.1 Hz), 4.87 (2H, s), 5.12 (2H, s), 6.36 (1H, dd, J = 1.5, 8.1 Hz), 6.48-6.63 (3H, m), 6.78 (1H, d, J = 6.6 Hz), 6.94-7.00 (2H, m), 7.17 (1H, d, J = 8.1 Hz), 7.42 (2H, d, J = 8.1 Hz), 7.92-8.01 (3H, m), 9.46 (1H, s), 9.61 (1H, s).
IR (KBr) cm-1 = 3335, 1616, 1528, 1503, 1456, 1311, 864, 751.

(0261)
Example 93.
N-(2-aminophenyl)-4-(N'-(3-nitrophenyl) thioureide methyl) benzamide (Table-1 = compound number 20).

Mp. 160 deg C (dec.).

1H NMR (270 MHz, DMSO-d6) delta ppm: 4.87 (2H, d, J = 5.1 Hz), 7.27-7.33 (3H, m), 7.46-7.63 (5H, m), 7.89-7.95 (2H, m), 8.05 (2H, d, J = 8.1 Hz), 8.70 (1H, s), 8.84 (1H, t, J = 8.9 Hz), 10.37 (1H, s).

(0262)

Example 94.

N-(2-amino-5-fluoro phenyl)-4-(N'-(pyridin-3-yl) methyl ureide methyl) benzamide (Table-1 = compound number 112).

Mp. (amorphous).

1H-NMR (270 MHz, DMSO-d6) = 4.77 (4H, d, J = 5.1 Hz), 4.85 (2H, s), 6.81 (2H, m), 7.16 (1H, dd, J = 2.9, 10.3 Hz), 7.39 (1H, dd, J = 5.1, 8.1 Hz), 7.53 (2H, d, J = 8.1 Hz), 7.81 (1H, d, J = 8.1 Hz), 7.93 (2H, d, J = 8.1 Hz), 8.51 (1H, dd, J = 1.5, 5.1 Hz), 8.62 (1H, d, J = 1.5 Hz), 9.66 (1H, s).

IR (KBr) cm-1 = 3399, 1730, 1638, 1508, 1444, 1411.

(0263)

Example 95.

N-(2-hydroxyphenyl)-4-(N'-(pyridin-3-yl) methyl ureide methyl) benzamide (Table-1 = compound number 114).

Mp. (amorphous).

1H-NMR (270 MHz, DMSO-d6) = 4.43 (2H, d, J = 6.6 Hz), 4.69 (2H, s), 6.83 (1H, t, J = 6.6 Hz), 6.91 (1H, d, J = 8.1 Hz), 7.68 (1H, d, J = 6.6 Hz), 7.82 (2H, d, J = 8.1 Hz), 8.21 (1H, d, J = 4.4 Hz), 8.35 (1H, d, J = 2.2 Hz), 8.81 (1H, t, J = 6.6 Hz), 9.48 (1H, s), 9.75 (1H, s).

IR (KBr) cm-1 = 3399, 1684, 1535, 1236, 1064.

(0264)

Example 96.

Synthesis of N-(2-aminophenyl)-4-(2-(N-(pyridin-3-yl) acetylamino) ethyl) benzamide (Table-1 = compound number 77).

(96-1) .

Thionyl chloride (4 ml) was added to toluene (25 ml) suspension of terephthalaldehydic acid 3.40 g (22.6 mmol), and it was heated with stirring at 80 degrees for 2 hours. It was allowed to cool, and thereafter the residue from which the solvent was eliminated by distillation was dissolved in THF (50 ml), and acid chloride was prepared. Triethylamine (6 ml, 42.8 mmol) was added to THF (10 ml) solution of compound 4.16 g (20.0 mmol) of Step (1-2) of Example 1, and furthermore, the acid chloride which was prepared beforehand was dropwise added under ice cooling over a period of 30 minutes.

(0265)

Saturated aqueous sodium bicarbonate was added after stirring for five hours and was extracted with ethyl acetate. Saturated aqueous sodium chloride solution was washed organic layer, and next it was dried, and the residue obtained by elimination of the solvent by distillation was refined by silica gel column chromatography (chloroform to chloroform:ethyl acetate = 10:1), and N-(2-(N-tert-butoxycarbonyl) aminophenyl)-4-formyl benzamide 3.42 g (yield 50.2 %) were obtained as the pale-brown solid.

1H NMR (270 MHz, CDCl3) delta ppm: 1.52 (9H, s), 6.77 (1H, br.s), 7.16-7.18 (2H, m), 7.23-7.26 (1H, m), 7.88 (1H, d, J = 8.8 Hz), 7.98 (2H, d, J = 8.8 Hz), 8.13 (2H, d, J = 8.8 Hz), 9.57 (1H, br.s), 10.11 (1H, br.s).

IR (KBr) cm-1 = 3326,3251, 1707, 1696, 1659, 1603, 1165.

(0266)

(96-2) .

Toluene (10 ml) suspension of compound 3.0 g (8.82 mmol) step (96-1) and ethoxycarbonylmethyl triphenylphosphine 4.5 g (12.9 mmol) were stirred under a stream of nitrogen at 80 degrees for five hours 30 minutes. It was allowed to cool and thereafter it was diluted with ethyl acetate and next, it was washed with saturated aqueous sodium bicarbonate, water, saturated aqueous sodium chloride solution and was dried. The residue obtained by elimination of the solvent by distillation was refined by silica gel column chromatography (chloroform:ethyl acetate = 20:1), and ethyl 4-(N-(2-(N-tert-butoxycarbonyl) aminophenyl) aminocarbonyl) cinnamate 3.3 g (yield 91.1 %) were obtained as the yellow amorphous state solid.

1H NMR (270 MHz, CDCl3) delta ppm: 1.35 (3H, t, J = 7.3 Hz), 1.52 (9H, s), 4.28 (2H, q, J = 7.3 Hz), 6.52 (1H, d, J = 15.1 Hz), 6.80 (1H, br.s), 7.16-7.25 (3H, m), 7.61 (2H, d, J = 8.1 Hz), 7.71 (1H, d, J = 15.1 Hz), 7.82 (1H, d, 7.3 Hz), 7.98 (2H, d, J = 8.1 Hz), 9.34 (1H, br.s).

(0267)

(96-3) .

10 % Pd / C (water containing 0.5 g) was added under a stream of nitrogen to THF (30 ml)-methanol (40 ml) solution of compound 2.50 g (6.09 mmol) of step (96-2) and thereafter the mixture was stirred for under a stream of hydrogen 30 minutes. It was purged with nitrogen, and next, catalyst was filtered. Diisopropyl ether was added to the residue from which the solvent of the filtrate was eliminated by distillation, and the precipitated solid was recovered by filtration, and N-(2-[N-tert-butoxycarbonyl] aminophenyl)-4-(2-ethoxycarbonyl ethyl) benzamide 2.23 g (yield 88.8 %) were obtained as white solid by drying.

1H NMR (270 MHz, CDCl3) delta ppm: 1.25 (3H, t, J = 7.3 Hz), 1.52 (9H, s), 2.65 (2H, t, J = 7.3 Hz), 3.02 (2H, t, J = 7.3 Hz), 4.13 (2H, q, J = 7.3 Hz), 6.77 (1H, br.s), 7.16-7.33 (5H, m), 7.78 (1H, d, J = 8.1 Hz), 7.89 (2H, d, J = 8.8 Hz), 9.06 (1H, br.s).

(0268)

(96-4) .

Lithium hydroxide monohydrate 0.37 g (8.82 mmol) were added to methanol (10 ml)-water (15 ml) suspension of compound 2.21 g (5.36 mmol) step (96-3) and the mixture was stirred at 40 degrees for three hours. It was allowed to cool, thereafter, 10 % hydrochloric acid aqueous solution was added and it was extracted with ethyl acetate. By wash organic layer with saturated aqueous sodium chloride solution, and thereafter is dried, and is added diisopropyl ether in the residue obtained by elimination of the solvent by distillation, and is recovered by filtration the precipitated solid, and drying, thereby N-(2-(N-tert-butoxycarbonyl) aminophenyl)-4-(2-carboxyethyl) benzamide 1.87 g (yield 90.8 %) were obtained as white solid.

1H NMR (270 MHz, DMSO-d6) delta ppm: 1.45 (9H, s), 2.59 (2H, t, J = 7.3 Hz), 2.91 (2H, t, J = 7.3 Hz), 7.13-7.20 (2H, m), 7.40 (2H, d, J = 8.1 Hz), 7.54 (2H, dd, J = 7.3, 2.1 Hz), 7.88 (2H, d, J = 8.1 Hz), 8.66 (1H, br.s), 9.79 (1H, br.s).

(0269)

(96-5) .

Triethylamine 0.1 ml (0.7 mmol) and molecular sieve 4 A 0.3 g were added to benzene (5 ml) suspension of compound 0.12 g (0.3 mmol) of step (96-4) and the mixture was stirred under a stream of nitrogen for 30 minutes. Diphenylphosphoryl azide 0.15 ml (0.7 mmol) were added into this solution and it was heated under reflux for two hours. It was allowed to cool and thereafter benzyl alcohol 0.4 ml (3.8 mmol) were added and furthermore were heated under reflux for 2 hours 30 minutes. It was diluted with ethyl acetate and next, was washed with water and with saturated aqueous sodium chloride solution.

(0270)

The organic layer was dried, and thereafter the residue obtained by elimination of the solvent by distillation was refined by silica gel column chromatography (chloroform:ethyl acetate = 4:1), thereby N-(2-(N-tert-butoxycarbonyl) aminophenyl)-4-(2-(N-benzyloxycarbonylamino) ethyl) benzamide 129 mg (88 %) were obtained as a colourless oily substance.

1H NMR (270 MHz, CDCl3) delta ppm: 1.51 (9H, s), 2.89 (2H, t, J = 7.3 Hz), 3.45-3.54 (2H, m), 4.80 (1H, m), 5.10 (2H, s), 6.76 (1H, br.s), 7.20-7.38 (10H, m), 7.79 (1H, d, J = 8.8 Hz), 7.89 (2H, d, J = 8.1 Hz), 9.10 (1H, br.s).

(0271)

(96-6).

10 % Pd / C (contains water, 0.05 g) was added under a stream of nitrogen to methanol (10 ml) solution of compound 129 mg (0.26 mmol) of step (96-5) and the mixture was stirred under a stream of hydrogen for two hours. Catalyst was eliminated by distillation, and next, obtained residue was dissolved dichloromethane (5 ml) by drying. 3-pyridine acetic acid salt acid salt 0.18 g (1.04 mmol) were added to this solution, and furthermore triethylamine 0.28 g (2.0 mmol) were added, and it was cooled with ice. 2-chloro-1,3-dimethyl imidazolinium chloride 0.17 g (1.0 mmol) were added under ice cooling and were stirred for two hours. Saturated aqueous sodium bicarbonate was added and thereafter was extracted with chloroform. Organic layer was washed with saturated aqueous sodium chloride solution, and thereafter it was dried, and the residue obtained by elimination of the solvent by distillation was refined by silica gel column chromatography (ethyl acetate:methanol = 10:1), thereby N-(2-(N-tert-butoxycarbonyl)

aminophenyl)-4-(2-(N-(pyridin-3-yl) acetylamino) ethyl) benzamide 50 mg (yield 40 %) were obtained as a colourless oily substance.

(0272)
1H NMR (270 MHz, CDCl3) delta ppm: 1.48 (9H, s), 2.80 (2H, t, J = 6.6 Hz), 3.42 (2H, m), 3.52 (2H, s), 6.33 (1H, t-like, J = 5.9 Hz), 7.09 (2H, d, J = 8.1 Hz), 7.14-7.20 (2H, m), 7.24 (1H, dd, J = 4.4, 7.3 Hz), 7.41 (1H, dd, J = 3.7, 5.9 Hz), 7.50 (1H, s), 7.58 (1H, dd, J = 1.5, 5.9 Hz), 7.69 (1H, dd, J = 3.7, 5.9 Hz), 7.75 (2H, d, J = 8.1 Hz), 8.22 (1H, d, J = 2.1 Hz), 8.44 (1H, dd, J = 1.5, 4.4 Hz), 9.49 (1H, br.s).

(0273)
(96-7) .
4 N hydrochloric acid-dioxane (2 ml) was added to dioxane (2 ml)-methanol (1 ml) solution of compound 50 mg (0.10 mmol) of step (96-6) and the mixture was stirred for 2 hours 30 minutes at room temperature. Saturated aqueous sodium bicarbonate was added and thereafter was extracted with ethyl acetate. Organic layer was washed with saturated aqueous sodium chloride solution, and thereafter it was dried, and the residue obtained by elimination of the solvent by distillation was dried, thereby N-(2-aminophenyl)-4-(2-(N-(pyridin-3-yl) acetylamino) ethyl) benzamide 22 mg (yield 59 %) were obtained as the amorphous state solid.

(0274)
Mp. (amorphous) .1H NMR (270 MHz, DMSO-d6) delta ppm: 2.70-2.90 (4H, m), 3.42 (2H, s), 4.89 (2H, br.s), 6.60 (1H, dd, J = 7.3, 7.3 Hz), 6.78 (1H, d, J = 7.3 Hz), 6.97 (1H, dd, J = 7.3, 7.3 Hz), 7.16 (1H, d, J = 7.3 Hz), 7.29-7.32 (3H, m), 7.59 (1H, d, J = 8.1 Hz), 7.89 (1H, d, J = 8.1 Hz), 8.22 (1H, t-like), 8.41-8.43 (2H, m), 9.62 (1H, br.s).

(0275)
Example 97.
Synthesis of N-(2-aminophenyl)-4-(2-(N-(3-picoryl) aminocarbonyl) ethyl) benzamide (Table-1 = compound number 80).

(97-1) .

To dichloromethane (5 ml) suspension of compound 0.58 g step of Example 96 (96-4) (1.5 mmol), 3-picoryl amine 0.22 g (2.0 mmol) and triethylamine 0.56 ml (4.0 mmol) were added. Dichloromethane (5 ml) solution of 2-chloro-1,3-dimethyl imidazolinium chloride 0.39 g (2.0 mmol) was added under ice cooling and was stirred 1 hour 30 minutes. Saturated aqueous sodium bicarbonate was added and thereafter it was extracted with chloroform.

(0276)
The organic layer was washed with water, saturated aqueous sodium chloride solution, and thereafter it was dried, and the residue obtained by elimination of the solvent by distillation, was refined by silica gel column chromatography (chloroform:methanol:ammonia water = 100:10:1), thereby N-(2-(N-tert-butoxycarbonyl) aminophenyl)-4-(2-(N-(3-picoryl) aminocarbonyl) ethyl) benzamide 0.71 g (yield 94 %) were obtained as pale-brown oily substance.

1H NMR (270 MHz, CDCl3) delta ppm: 1.45 (9H, s), 2.42 (2H, t, J = 7.3 Hz), 2.98 (2H, t, J = 7.3 Hz), 4.32 (2H, d, J = 6.6 Hz), 6.44 (1H, t, J = 6.6 Hz), 7.14-7.27 (5H, m), 7.48-7.57 (3H, m), 7.63-7.68 (3H, m), 7.90 (1H, d, J = 2.1 Hz), 8.43 (1H, dd, J = 1.4, 4.4 Hz), 9.86 (1H, br.s).

(0277)
(97-2) .
4 N hydrochloric acid-dioxane (5 ml) was added to dioxane (5 ml) solution of compound 0.70 g (1.47 mmol) of step (97-1) and furthermore methanol (2 ml) was added and was stirred at room temperature for two hours. Saturated aqueous sodium bicarbonate was added and thereafter was extracted with ethyl acetate. The organic layer was washed with saturated aqueous sodium chloride solution, and thereafter it was dried, and diisopropyl ether was added with the residue obtained by elimination of the solvent by distillation, and the precipitated solid was recovered by filtration, and N-(2-aminophenyl)-4-(2-(N-(3-picoryl) aminocarbonyl) ethyl) benzamide 0.42 g (yield 76.3 %) were obtained as the opal solid by drying.

(0278)
Mp. 168-170 deg C.
1H NMR (270 MHz, DMSO-d6) delta ppm: 2.47-2.53 (2H, m), 2.93 (2H, t, J = 7.3 Hz), 4.27 (2H, d, J = 5.9 Hz), 4.90 (2H, br.s), 6.60 (1H, dd, J = 7.3, 7.3 Hz), 6.78 (1H, d, J = 8.1 Hz), 6.97 (1H,

dd, J = 6.6, 7.3 Hz), 7.16 (1H, d, J = 6.6 Hz), 7.28-7.35 (1H, m), 7.33 (2H, d, J = 8.1 Hz), 7.49 (1H, dd, J = 2.1, 5.9 Hz), 7.89 (2H, d, J = 8.1 Hz), 8.39-8.44 (3H, m), 9.62 (1H, br.s).
IR (KBr) cm-1 = 3313, 1641, 1523, 1457, 1300, 748, 713.

(0279)
Example 98.
Synthesis of N-(2-aminophenyl)-4-((pyridin-3-yl) methylamino carbonyl oxymethyl) benzamide (Table-1 = compound number 85).

(98-1) .
N,N'-carbonyldiimidazole 1.78 g (11.0 mmol) were added at room temperature to THF (20 ml) solution of methyl 4-hydroxymethyl benzoate 1.99 g (12.0 mmol), and the mixture was stirred for one hour. 3-picoryl amine 1.08 g (10.0 mmol) were added at room temperature into this solution and were stirred 3 hours 30 minutes, and next, it was left to stand overnight. Water was added to this, and it was diluted, and next, it was extracted with ethyl acetate.

(0280)
The organic layer was washed with saturated aqueous sodium chloride solution, and thereafter it was dried, and the residue obtained by elimination of the solvent by distillation was refined by silica gel column chromatography (ethyl acetate), and N-(4-methoxycarbonyl) benzyloxycarbonyl-3-picoryl amine 2.76 g (yield 91.9 %) were obtained as the white wax state solid.

1H NMR (270 MHz, CDCl3) delta ppm: 3.91 (3H, s), 4.40 (2H, d, J = 5.9 Hz), 5.18 (2H, s), 5.50 (1H, br.s), 7.24-7.28 (1H, m), 7.40 (2H, d, J = 8.1 Hz), 7.65 (1H, d, J = 7.3 Hz), 8.02 (2H, d, J = 8.8 Hz), 8.50-8.53 (2H, m).

(0281)
(98-2) .
To methanol (10 ml)-water (20 ml) suspension of compound 2.40 g (8.0 mmol) of step (98-1), lithium hydroxide monohydrate 0.42 g (10.0 mmol) were added and were stirred at room temperature for five hours. 10 % hydrochloric acid aqueous solution was added, and it was made

acidic (pH 2-4), and next, the precipitated solid was recovered by filtration, and, by drying, N-(4-carboxy) benzyloxycarbonyl-3-picoryl amine 1.83 g (yield 79.9 %) were obtained as white solid.

1H NMR (270 MHz, DMSO-d6) delta ppm: 4.24 (2H, d, J = 5.9 Hz), 5.13 (2H, s), 7.33-7.38 (1H, m), 7.46 (2H, d, J = 8.1 Hz), 7.94 (2H, d, J = 8.1 Hz), 7.95-8.01 (1H, m), 8.46 (1H, d, J = 5.1 Hz), 8.49 (1H, d, J = 1.5 Hz), 13.0 (1H, br.s).

(0282)
(98-3) .
Oxalyl chloride 1.0 ml (11.4 ml) were gradually added to dichloromethane (20 ml) suspension of compound 1.26 g (4.4 mmol) of step (98-2) and furthermore several drops DMF were added, thereafter the mixture was stirred at room temperature for ten minutes furthermore at 40 degrees for 30 minutes. It was allowed to cool, and thereafter the solvent was eliminated by distillation, and further excess oxalyl chloride was eliminated by distillation with toluene. Dichloromethane (10 ml) was added to this residue, and thereafter it was cooled with ice, and furthermore dichloromethane (8 ml)-pyridine (8 ml) solution of compound 0.83 g (4.0 mmol) obtained in Step (1-2) of Example 1 was added dropwise. Next, the mixture was stirred for seven hours while being warmed to room temperature, and it was left to stand overnight.

(0283)
Saturated aqueous sodium bicarbonate was added and thereafter was extracted with chloroform. Organic layer was washed with saturated aqueous sodium chloride solution, and thereafter it was dried, and toluene was added to the residue obtained by elimination of the solvent by distillation. Furthermore excess pyridine was formed into an azeotrope, the obtained residue was refined by silica gel column chromatography (ethyl acetate), thereby N-(2-(N-tert-butoxycarbonyl) aminophenyl)-4-((pyridin-3-yl) methylamino carbonyl oxymethyl) benzamide 1.40 g (yield 73.4 %) were obtained as the pale-brown solid.

1H NMR (270 MHz, CDCl3) delta ppm: 1.51 (9H, s), 4.40 (2H, d, J = 5.9 Hz), 5.19 (2H, s), 5.56 (1H, m), 7.07 (1H, br.s), 7.14-7.31 (4H, m), 7.43 (2H, d, J = 8.1 Hz), 7.65 (1H, d, J = 8.1 Hz), 7.76 (1H, d, J = 7.3 Hz), 7.95 (2H, d, J = 8.1 Hz), 8.52 (2H, d, J = 4.1 Hz), 9.32 (1H, br.s).

(0284)

(98-4) .

4 N hydrochloric acid-dioxane (9 ml) was added at room temperature into dioxane (10 ml)-methanol (2 ml) solution of compound 1.00 g (2.10 mmol) of step (98-3) and was stirred for two hours. Saturated aqueous sodium bicarbonate was added and thereafter was extracted with ethyl acetate-methyl ethyl ketone (1:1). Organic layer was washed with saturated aqueous sodium chloride solution, and thereafter it was dried, and the solvent was eliminated by distillation, and methanol-diisopropyl ether was added to obtained residue, and the formed solid was recovered by filtration, and N-(2-aminophenyl)-4-((pyridin-3-yl) methylamino carbonyl oxymethyl) benzamide 0.79 g (quantitative) were obtained as white solid by drying.

(0285)

Mp. 139-141 deg C.

1H NMR (270 MHz, DMSO-d6) delta ppm: 4.25 (2H, d, J = 5.9 Hz), 4.90 (2H, s), 5.13 (2H, s), 6.60 (1H, dd, J = 6.6, 7.3 Hz), 6.78 (1H, d, J = 7.3 Hz), 6.97 (1H, dd, J = 6.6, 7.3 Hz), 7.17 (1H, d, J = 7.3 Hz), 7.36 (1H, dd, J = 4.4, 8.1 Hz), 7.47 (2H, d, J = 8.1 Hz), 7.67 (1H, d, J = 8.1 Hz), 7.97 (2H, d, J = 7.3 Hz), 7.90-8.00 (1H, m), 8.46 (1H, dd, J = 1.5, 5.1 Hz), 8.49 (1H, d, J = 2.1 Hz), 9.65 (1H, br.s).

IR (KBr) cm-1 = 3326 (br), 1694, 1637, 1526, 1458, 1147, 750, 712.

(0286)

Example 99.

N-(2-aminophenyl)-4-(3-(imidazole-1-yl) propylamino carbonyl oxymethyl) benzamide (Table-1 = compound number 215).

It was synthesised by process same as in Example 98.

Mp. (amorphous).

1H NMR (270 MHz, DMSO-d6) delta ppm: 1.80-1.89 (2H, m), 2.94-3.02 (2H, m), 3.98 (2H, t, J = 7.3 Hz), 4.88 (2H, s), 5.11 (2H, s), 6.55-6.63 (1H, m), 6.76-6.97 (3H, m), 7.10-7.18 (2H, m), 7.43-7.48 (3H, m), 7.61 (1H, s), 7.98 (2H, d, J = 8.1 Hz), 9.66 (1H, s).

(0287)

Example 100.

Synthesis of N-(2-aminophenyl)-4-(phenylacetyl amino) benzamide (Table-1 = compound number 2)

(100-1)
Triethylamine 16.8 ml (120 mmol) were added to dichloromethane (120 ml) solution of compound 16.6 g (80 mmol) obtained with Step (1-2) of Example 1, and furthermore dichloromethane (40 ml) solution of 4-nitrobenzoyl chloride 16.0 g (86.4 mmol) was gradually added under ice cooling and thereafter the mixture was stirred for seven hours. Saturated aqueous sodium bicarbonate was added and thereafter it was extracted with chloroform.

(0288)
The organic layer was washed with 1 N hydrochloric acid aqueous solution, saturated aqueous sodium bicarbonate, saturated aqueous sodium chloride solution, and next, it was dried, and the solvent was eliminated by distillation. By washing obtained residue with diisopropyl ether, N-(2-(N-tert-butoxycarbonyl amino) phenyl)-4-nitrobenzamide 28.0 g (yield 98 %) were obtained as the straw-coloured solid.

1H NMR (270 MHz, CDCl3) delta ppm: 1.53 (9H, s), 7.17-7.29 (4H, m), 7.85 (1H, br.d, J = 7.3 Hz), 8.17 (2H, d, J = 8.8 Hz), 8.32 (2H, d, J = 8.8 Hz), 9.88 (1H, br.s).

(0289)
(100-2) .
10 % Pd / C (water containing, 2.4 g) was added under a stream of nitrogen to THF (80 ml)-methanol (80 ml) mixed solution of compound 24.0 g (67.2 mmol) obtained with step (100-1) and the mixture was stirred under a stream of hydrogen for one hour 30 minutes. Absorption of hydrogen stopped, and next, catalyst was separated by filtration, and diisopropyl ether and ethyl acetate were added in the residue obtained by elimination of the solvent by distillation, and obtained solid was recovered by filtration, and N-(2-(N-tert-butoxycarbonyl amino) phenyl)-4-amino benzamide 18.96 g (yield 86 %) were obtained as white solid by drying.

1H NMR (270 MHz, DMSO-d6) delta ppm: 1.46 (9H, s), 5.84 (2H, s), 6.61 (2H, d, J = 8.8 Hz), 7.10-7.18 (2H, m), 7.46-7.55 (2H, m), 7.68 (2H, d, J = 8.8 Hz), 8.67 (1H, s), 9.49 (1H, s).

(0290)

(100-3) .

Into methylene chloride (15 ml) solution of compound 1.6 g (4.88 mmol) obtained with step (100-2), were added pyridine 0.8 ml (9.9 mmol) and phenylacetyl chloride 0.96 ml (7.26 mmol) and the mixture was stirred for one day. On completion of the reaction, water was added, and the precipitated crystals were recovered by filtration, and N-(2-(N-tert-butoxycarbonyl amino) phenyl)-4-(phenylacetyl amino) benzamide 1.66 g (yield 76 %) were obtained.

(0291)

(100-4) .

Iodotrimethylsilane 0.88 ml (6.18 mmol) were added at room temperature to acetonitrile solution (25 ml) of compound 1 g (2.24 mmol) obtained with step (100-3) and the mixture was stirred for three hours. On completion of the reaction, the solvent was concentrated, and obtained residue was recrystallised from methanol, and N-(2-aminophenyl)-4-(phenylacetyl amino) benzamide 0.29 g (yield 38 %) were obtained as the white crystals.

(0292)

Mp. 232-237 deg C.

1H NMR (270 MHz, DMSO-d6) delta ppm: 3.69 (2H, s), 4.90 (2H, s), 6.60 (1H, t, J = 7.3 Hz), 6.77 (1H, d, J = 7.3 Hz), 6.96 (1H, t, J = 7.3 Hz), 7.15 (1H, d, J = 7.4 Hz), 7.22-7.35 (5H, m), 7.72 (2H, d, J = 8.8 Hz), 7.95 (2H, d, J = 8.8 Hz), 9.57 (1H, s), 10.43 (1H, s).

IR (KBr) cm-1 = 2937, 2764, 1660, 1598, 1506, 1459.

(0293)

By process same as in Example 100, the compounds of Example 101 to Example 128 were synthesised. Below melting point (mp.) of the compound, 1H NMR, measured value of IR are shown.

(0294)

Example 101.

N-(2-aminophenyl)-4-((4-phenyl butanoyl) amino) benzamide (Table-1 = compound number 4).

Mp. (amorphous).

1H NMR (270 MHz, DMSO-d6) delta ppm: 1.91 (2H, hep, J = 7.3 Hz), 2.37 (2H, t, J = 7.3 Hz), 2.64 (2H, t, J = 7.3 Hz), 5.0 (2H, br.s), 6.61 (1H, t, 7.0 Hz), 6.79 (1H, dd, J = 1.5, 8.1 Hz), 6.97 (1H, t, J = 7.0 Hz), 7.10-7.40 (6H, m), 7.71 (2H, d, J = 8.8 Hz), 7.94 (2H, d, J = 8.8 Hz), 9.57 (1H, s), 10.15 (1H, s).
IR (KBr) cm-1;3344, 1687, 1603, 1542, 1460, 1315, 1033, 842, 737.

(0295)
Example 102.
N-(2-aminophenyl)-4-((4-chlorophenyl acetyl) amino) benzamide (Table-1 = compound number 15).

Mp. (amorphous).
1H NMR (270 MHz, DMSO-d6) delta ppm: 3.72 (2H, s), 7.29-7.43 (8H, m), 7.77 (2H, d, J = 8.8 Hz), 8.00 (2H, d, J = 8.8 Hz), 10.29 (1H, s), 10.52 (1H, s).
IR (KBr) cm-1 = 3300, 2868, 1664, 1638, 1520.

(0296)
Example 103.
N-(2-aminophenyl)-4-((2-nitrophenyl acetyl) amino) benzamide hydrochloride (hydrochloride of Table-1 = compound number 19).

Mp. (amorphous).
1H NMR (270 MHz, DMSO-d6) delta ppm: 4.20 (2H, s), 7.20-7.30 (3H, m), 7.40-7.45 (1H, m), 7.60 (2H, d), 7.71-7.77 (3H, m), 8.02-8.10 (4H, m), 10.27 (1H, br.s), 10.64 (1H, br.s).
IR (KBr) cm-1 = 3263, 1676, 1647, 1518, 1184, 759.

(0297)
Example 104.
N-(2-aminophenyl)-4-((4-nitrophenyl acetyl) amino) benzamide (Table-1 = compound number 21).

Mp. 222-226 deg C.

1H NMR (270 MHz, DMSO-d6) delta ppm: 3.90 (2H, s), 4.96 (2H, br.s), 6.60 (1H, dt, J = 1.5, 6.6 Hz), 6.78 (1H, dd, J = 1.5, 6.6 Hz), 6.97 (1H, dt, J = 1.5, 6.6 Hz), 7.15 (1H, dd, J = 1.5, 6.6 Hz), 7.63 (2H, d, J = 8.8 Hz), 7.71 (2H, d, J = 8.8 Hz), 7.95 (2H, d, J = 8.8 Hz), 8.22 (2H, d, J = 8.8 Hz), 9.59 (1H, s), 10.54 (1H, s).
IR (KBr) cm-1 = 3395, 3334, 1671, 1630, 1519, 1346.

(0298)
Example 105.
N-(2-aminophenyl)-4-((2-aminophenyl acetyl) amino) benzamide (Table-1 = compound number 22).

Mp. 177-182 deg C (dec.).
1H NMR (270 MHz, DMSO-d6) delta ppm: 3.54 (2H, s), 4.88 (2H, br.s), 5.09 (2H, br.s), 6.55 (1H, dd, J = 6.6, 7.3 Hz), 6.59 (1H, dd, J = 7.3, 7.3 Hz), 6.68 (1H, d, J = 7.3 Hz), 6.78 (1H, d, J = 7.3 Hz), 6.96 (2H, dd, J = 7.3, 7.3 Hz), 7.06 (1H, d, J = 6.6 Hz), 7.15 (1H, d, J = 7.3 Hz), 7.71 (2H, d, J = 8.8 Hz), 7.95 (2H, d, J = 8.8 Hz), 9.57 (1H, br.s), 10.39 (1H, br.s).
IR (KBr) cm-1 = 3374, 3256 (br.), 1683, 1597, 1503, 1317, 1262, 1180, 1153, 747.

(0299)
Example 106.
N-(2-aminophenyl)-4-((4-aminophenyl acetyl) amino) benzamide (Table-1 = compound number 26).

Mp. 219-226 deg C (dec.).
1H NMR (270 MHz, DMSO-d6) delta ppm: 3.46 (2H, s), 4.93 (4H, br.s), 6.52 (2H, d, J = 8.1 Hz), 6.59 (1H, dt, J = 1.5, 7.3 Hz), 6.77 (1H, dd, J = 1.4, 7.3 Hz), 6.97 (1H, dt, J = 1.4, 7.3 Hz), 6.99 (2H, d, J = 8.1 Hz), 7.15 (1H, dd, J = 1.5, 7.3 Hz), 7.70 (2H, d, J = 8.8 Hz), 7.93 (2H, d, J = 8.8 Hz).
IR (KBr) cm-1 = 3278, 3032, 1675, 1628, 1516.

(0300)
Example 107.

N-(2-aminophenyl)-4-((4-methoxyphenyl acetyl) amino) benzamide (Table-1 = compound number 32).

Mp. (amorphous).
1H NMR (270 MHz, DMSO-d6) delta ppm: 3.62 (2H, s), 3.74 (3H, s), 6.90 (2H, d, J = 8.8 Hz), 7.26 (2H.d.J = 8.8 Hz), 7.30 (3H, m), 7.39 (1H, m), 7.77 (2H, d, J = 8.8 Hz), 7.99 (2H, d, J = 8.8 Hz), 10.26 (1H, s), 10.44 (1H, s).
IR (KBr) cm-1 = 3300,2759, 1670, 1638, 1514, 1250.

(0301)
Example 108.
N-(2-aminophenyl)-4-((4-(N,N-dimethylamino) phenylacetyl) amino) benzamide (Table-1 = compound number 53).

Mp. 140 deg C.
1H NMR (270 MHz, DMSO-d6) delta ppm: 3.04 (6H, s), 3.67 (2H, s), 7.16 (2H, d, J = 8.1 Hz), 7.29-7.40 (6H, m), 7.76 (2H, d, J = 8.8 Hz), 7.99 (2H, d, J = 8.8 Hz), 10.29 (1H, s), 10.47 (1H, s).
IR (KBr) cm-1 = 3244, 2951, 2639, 1647, 1599, 1507.

(0302)
Example 109.
N-(2-aminophenyl)-4-((4-trifluoromethylphenyl acetyl) amino) benzamide (Table-1 = compound number 43).

Mp. (amorphous).
1H NMR (270 MHz, DMSO-d6) delta ppm: 3.84 (2H, s), 6.89 (1H, t, J = 7.4 Hz), 7.00 (1H, d, J = 7.4 Hz), 7.11 (1H, t, J = 7.4 Hz), 7.25 (1H, d, J = 7.4 Hz), 7.57 (2H, d, J = 8.8 Hz), 7.71 (2H, d, J = 8.8 Hz), 7.73 (2H, d, J = 8.8 Hz), 7.97 (2H, d, J = 8.8 Hz), 9.87 (1H, s), 10.54 (1H, s).
IR (KBr) cm-1 = 3260, 1664, 1605, 1521, 1327, 1119.

(0303)
Example 110.

N-(2-aminophenyl)-4-((pyridin-2-yl) acetylamino) benzamide dihydrochloride (hydrochloride of Table-1 = compound number 174).

Mp. (amorphous).
1H NMR (270 MHz, DMSO-d6) delta ppm: 4.60 (2H, s), 7.30-7.46 (3H, m), 7.56 (1H, d, J = 7.4 Hz), 7.79 (2H, d, J = 8.8 Hz), 7.95 (1H, t, J = 6.6 Hz), 8.01 (1H, d, J = 7.4 Hz), 8.11 (2H, d, J = 8.8 Hz), 8.49 (1H, t, J = 7.4 Hz), 8.87 (1H, d, J = 5.1 Hz), 10.46 (1H, s).

(0304)
Example 111.
N-(2-aminophenyl)-4-((pyridin-3-yl) acetylamino) benzamide dihydrochloride (hydrochloride of Table-1 = compound number 68).

Mp. 182-189 deg C (dec.).
1H NMR (270 MHz, DMSO-d6) delta ppm: 4.12 (2H, s), 7.29-7.59 (4H, m), 7.80 (2H, d, J = 8.8 Hz), 8.05 (1H, m), 8.11 (2H, d, J = 8.8 Hz), 8.57 (1H, d, J = 8.1 Hz), 8.85 (1H, d, J = 5.2 Hz), 8.95 (1H, s), 10.25 (1H, s), 10.48 (1H, s).

(0305)
Example 112.
N-(2-aminophenyl)-4-((3-(pyridin-3-yl) propanoyl) amino) benzamide (Table-1 = compound number 69).

Mp. 184-186 deg C.
1H NMR (270 MHz, DMSO-d6) delta ppm: 2.80 (2H, t, J = 7.3 Hz), 3.08 (2H, t, J = 7.3 Hz), 6.87 (1H, t, J = 8.0 Hz), 6.99 (1H, dd, J = 1.4, 8.0 Hz), 7.11 (1H, dt, J = 1.4, 8.0 Hz), 7.25 (1H, d, J = 8.0 Hz), 7.70 (2H, d, J = 8.8 Hz), 7.77 (1H, dd, J = 5.8, 8.0 Hz), 7.96 (2H, d, J = 8.8 Hz), 8.22 (1H, d, J = 8.0 Hz), 8.75 (1H, d, J = 1.4 Hz), 9.83 (1H, s), 10.25 (1H, s).

(0306)
Example 113.
N-(2-aminophenyl)-2-chloro-4-(3-(pyridin-3-yl) propanoyl amino) benzamide (Table-1 = compound number 123).

Mp. (amorphous).
1H NMR (270 MHz, DMSO-d6) delta ppm: 2.70 (2H, t, J = 8.1 Hz), 2.96 (2H, t, J = 7.3 Hz), 4.74 (2H, br.s), 6.60 (1H, t, J = 6.6 Hz), 6.78 (1H, d, J = 6.6 Hz), 6.95 (1H, t, J = 6.6 Hz), 7.19 (1H, dd, J = 1.5, 7.3 Hz), 7.29 (1H, dd, J = 5.1, 7.3 Hz), 7.66 (2H, d, J = 8.8 Hz), 7.92 (2H, d, J = 8.8 Hz), 8.48 (1H, d, J = 2.2 Hz), 9.37 (1H, s), 10.00 (1H, s).
IR (KBr) cm-1 = 3273, 1675, 1519, 1315, 1181, 852, 747.

(0307)
Example 114.
N-(2-aminophenyl)-4-((N-(pyridin-3-yl) methyl-N-trifluoroacetylamino) acetylamino) benzamide (Table-1 = compound number 107).

Mp. 145 deg C (dec.).
1H NMR (270 MHz, DMSO-d6) delta ppm: 4.18 and 4.42 (total 2H, s), 4.73 and 4.83 (total 2H, s), 4.87 (2H, br.s), 6.60 (1H, dd, J = 7.3, 8.1 Hz), 6.78 (1H, d, J = 8.1 Hz), 6.96 (1H, dd, J = 7.3, 7.3 Hz), 7.16 (1H, d, J = 8.1 Hz), 7.35-7.45 (1H, m), 7.66 (2H, d, J = 5.9 Hz), 7.70-7.80 (1H, m), 7.90-8.00 (2H, m), 8.51-8.55 (1H, m), 8.58 (1H, s), 9.60 (1H, br.s), 10.36 and 10.43 (total 1H, br.s).

(0308)
Example 115.
N-(2-aminophenyl)-4-((N-(pyridin-3-yl) methylamino) acetylamino) benzamide (Table-1 = compound number 105).

Mp. 160 deg C (dec.).
1H NMR (270 MHz, DMSO-d6) delta ppm: 3.30 (2H, s), 3.79 (2H, s), 4.88 (2H, s), 6.60 (1H, dd, J = 7.3, 7.3 Hz), 6.78 (1H, d, J = 8.1 Hz), 6.97 (1H, dd, J = 7.3, 8.1 Hz), 7.16 (1H, d, J = 8.1 Hz), 7.74 (2H, d, J = 8.8 Hz), 7.80 (1H, d, J = 7.3 Hz), 7.95 (2H, d, J = 8.1 Hz), 8.46 (1H, d, J = 3.7 Hz), 8.57 (1H, s), 9.57 (1H, s), 10.08 (1H, br.s).
IR (KBr) cm-1 = 3298, 1693, 1637, 1602, 1544, 1454, 1262, 848, 762.

(0309)

Example 116.

N-(2-aminophenyl)-4-(N-(pyridin-3-yl) methyl oxamoyl amino) benzamide (Table-1 = compound number 104).

Mp. (amorphous).

1H NMR (270 MHz, DMSO-d6) delta ppm: 4.43 (2H, d, J = 6.6 Hz), 4.90 (2H, br.s), 6.60 (1H, dd, J = 6.6, 7.3 Hz), 6.78 (1H, d, J = 7.3 Hz), 6.97 (1H, ddd, J = 1.5, 6.6, 7.3 Hz), 7.16 (1H, d, J = 7.3 Hz), 7.37 (1H, dd, J = 4.4, 8.1 Hz), 7.73 (1H, d, J = 8.1 Hz), 7.96 and 7.96 (4H, AA'BB', J = 9.4 Hz), 8.47 (1H, dd, J = 1.5, 5.1 Hz), 8.56 (1H, d, J = 1.5 Hz), 9.59 (1H, s), 9.67 (1H, t, J = 6.6 Hz), 10.92 (1H, br.s).

IR (KBr) cm-1 = 3299, 1644, 1518, 1320, 1119, 748.

(0310)

Example 117.

N-(2-aminophenyl)-4-((N-(pyridin-3-yl) methyl-N-nicotinoyl amino) acetylamino) benzamide (Table-1 = compound number 106).

Mp. (amorphous).

1H NMR (270 MHz, DMSO-d6) delta ppm: 4.11 (major 2H, s), 4.26 (minor 2H, s), 4.75 (major 2H, s), 4.65 (minor 2H, s), 4.88 (total 2H, br.s), 6.60 (total 1H, dd, J = 7.3, 8.1 Hz), 6.78 (total 1H, d, J = 7.3 Hz), 6.97 (total 1H, dd, J = 7.3, 8.1 Hz), 7.15 (total 1H, d, J = 8.1 Hz), 7.41-7.95 (total 8H, m), 8.46-8.52 (total 1H, m), 8.63-8.70 (total 2H, m), 9.59 (total 1H, s), 10.22 (major 1H, br.s), 10.37 (minor 1H, br.s).

IR (KBr) cm-1 = 3269, 1701, 1637, 1603, 1534, 1506, 1312, 1254, 752.

(0311)

Example 118.

N-(2-aminophenyl)-4-((4-(pyridin-3-yl) butanoyl) amino) benzamide (Table-1 = compound number 70).

Mp. 165-167 deg C (dec.).

1H NMR (270 MHz, DMSO-d6) delta ppm: 1.88-1.99 (2H, m), 2.68 (2H, t, J = 7.3 Hz), 2.39 (2H, t, J = 7.3 Hz), 6.78-6.81 (1H, m), 6.94-6.99 (1H, m), 7.15-7.18 (1H, m), 7.34-7.39 (1H, m), 7.69-7.72 (3H, m), 7.94 (2h, d, J = 8.8 Hz), 8.43-8.48 (2H, m).
IR (KBr) cm-1 = 3291, 1660, 1626, 1308, 1261, 1182, 1027, 825, 747.

(0312)
Example 119.
N-(2-aminophenyl)-4-((N-(pyridin-3-yl) methyl-N-methylamino) acetylamino) benzamide (Table-1 = compound number 108)

mp. 154-155 deg C.
1H NMR (270 MHz, DMSO-d6) delta ppm: 2.28 (3H, s), 3.27 (2H, s), 3.71 (2H, s), 4.88 (2H, br.s), 6.60 (1H, dd, J = 6.6, 7.3 Hz), 6.78 (1H, d, J = 8.1 Hz), 6.97 (1H, dd, J = 7.3, 8.1 Hz), 7.16 (1H, d, J = 8.1 Hz), 7.38 (1H, dd, J = 2.9, 8.1 Hz), 7.77 (2H, d, J = 8.8 Hz), 7.75-7.85 (1H, m), 7.95 (2H, d, J = 8.8 Hz), 8.47 (1H, d, J = 1.5 Hz), 8.49 (1H, s), 9.56 (1H, s), 10.02 (1H, br.s).

(0313)
Example 120.
N-(2-aminophenyl)-4-(N-(pyridin-3-yl) oxy acetylamino) benzamide (Table-1 = compound number 65).

Mp. 175-179 deg C.
1H NMR (270 MHz, DMSO-d6) delta ppm: 4.86 (2H, s), 4.90 (2H, br.s), 6.60 (1H, d, J = 7.3, 7.3 Hz), 6.78 (1H, d, J = 7.3 Hz), 6.97 (1H, dd, J = 6.6, 7.3 Hz), 7.16 (1H, d, J = 8.1 Hz), 7.34-7.47 (2H, m), 7.76 (2H, d, J = 8.8 Hz), 7.98 (2H, d, J = 8.8 Hz), 8.22 (1H, d, J = 3.6 Hz), 8.39 (1H, d, J = 2.9 Hz), 9.60 (1H, br.s), 10.40 (1H, br.s).
IR (KBr) cm-1 = 3321, 1655, 1530, 1276, 1231, 1068, 757.

(0314)
Example 121.
N-(2-aminophenyl)-4-(4-(pyridin-3-yl)-1,4-dioxobutyl amino) benzamide (Table-1 = compound number 99).

Mp. 190-194 deg C.
1H NMR (270 MHz, DMSO-d6) delta ppm: 2.08 (2H, t, J = 6.4 Hz), 3.41 (2H, t, J = 6.4 Hz), 4.86 (2H, s), 6.59 (1H, t, J = 5.6 Hz), 6.78 (1H, d, J = 7.9 Hz), 6.96 (1H, t, J = 7.4 Hz), 7.15 (1H, d, J = 7 Hz), 7.58 (1H, dd, J = 4.9, 7.9 Hz), 7.70 (2H, d, J = 8.9 Hz), 7.94 (2H, d, J = 8.9 Hz), 8.35 (1H, d, J = 7.9 Hz), 8.81 (1H, d, J = 4 Hz), 9.18 (1H, s), 9.56 (1H, s), 10.32 (1H, s).
IR (KBr) cm-1 = 3317, 1691, 1652, 1601, 1522, 1312, 982, 847, 764, 701.

(0315)
Example 122.
N-(2-aminophenyl)-4-(3-(N-(pyridin-3-yl) amino)-1,3-dioxo propylamino) benzamide (Table-1 = compound number 94).

Mp. 196 deg C (dec.).
1H NMR (270 MHz, DMSO-d6) delta ppm: 3.57 (2H, s), 4.87 (2H, s), 6.57-6.62 (1H, m), 6.76-6.79 (1H, m), 6.94-6.99 (1H, m), 7.14-7.17 (1H, m), 7.33-7.38 (1H, m), 7.73 (2H, d, J = 8.8 Hz), 7.97 (2H, d, J = 8.8 Hz), 8.05-8.08 (1H, m), 8.27-8.30 (1H, m), 8.75-8.76 (1H, m), 9.59 (1H, s), 10.44 (1H, s), 10.47 (1H, s).
IR (KBr) cm-1 = 3410, 3315, 1685, 1655, 1625, 1536, 1428, 1362, 1263, 1201, 744.

(0316)
Example 123.
N-(2-aminophenyl)-4-(N-(pyridin-3-yl) methoxyacetyl amino)-3-methylbenzamide (Table-1 = compound number 102).

Mp. 178-181 deg C (dec.).
1H NMR (270 MHz, DMSO-d6) delta ppm: 2.28 (3H, s), 4.22 (2H, s), 4.71 (2H, s), 4.89 (2H, br.s), 6.60 (1H, dd, J = 7.3, 7.3 Hz), 6.78 (1H, d, J = 8.1 Hz), 6.97 (1H, dd, J = 7.3, 8.1 Hz), 7.16 (1H, d, J = 7.3 Hz), 7.43 (1H, dd, J = 4.4, 8.1 Hz), 7.71 (1H, d, J = 8.1 Hz), 7.79-7.89 (3H, m), 8.54 (1H, dd, J = 1.5, 4.4 Hz), 8.66 (1H, d, J = 1.5 Hz), 9.36 (1H, br.s), 9.60 (1H, br.s).
IR (KBr) cm-1 = 3394, 3269, 1683, 1630, 1593, 1521, 1460, 1131, 750, 716.

(0317)
Example 124.

N-(2-aminophenyl)-4-(N-(thiophen-3-yl) methoxyacetyl amino) benzamide (Table-1 = compound number 204).

Mp. 186-189 deg C.
1H NMR (270 MHz, DMSO-d6) delta ppm: 4.11 (2H, s), 4.63 (2H, s), 4.89 (2H, br.s), 6.60 (1H, dd, J = 7.3, 7.3 Hz), 6.78 (1H, d, J = 8.1 Hz), 6.97 (1H, dd, J = 7.3, 7.3 Hz), 7.12-7.19 (2H, m), 7.53-7.57 (2H, m), 7.78 (2H, d, J = 8.8 Hz), 7.95 (2H, d, J = 8.8 Hz), 9.58 (1H, br.s), 10.04 (1H, br.s).
IR (KBr) cm-1 = 3341,3248, 1694, 1631, 1611, 1506, 1314, 1126.

(0318)
Example 125.
N-(2-aminophenyl)-4-(N-methyl-N-(pyridin-3-yl) methoxyacetyl amino) benzamide (Table-1 = compound number 103).

Mp. 180-183 deg C (dec.).
1H NMR (270 MHz, DMSO-d6) delta ppm: 3.24 (3H, s), 4.08 (2H, br.s), 4.50 (2H, s), 4.94 (2H, br.s), 6.60 (1H, dd, J = 7.3, 7.3 Hz), 6.79 (1H, d, J = 8.1 Hz), 6.98 (1H, dd, J = 7.3, 8.1 Hz), 8.03 (1H, d, J = 8.1 Hz), 8.48-8.50 (2H, m), 9.72 (1H, br.s).
IR (KBr) cm-1 = 3395,3283, 1683, 1639, 1604, 1506, 1459, 1307, 1124.

(0319)
Example 126.
N-(2-aminophenyl)-4-(N-(pyridin-2-yl) methoxyacetyl amino) benzamide (Table-1 = compound number 176).

Mp. 171-173 deg C.
1H NMR (270 MHz, DMSO-d6) delta ppm: 4.26 (2H, s), 4.74 (2H, s), 4.89 (2H, br.s), 6.60 (1H, dd, J = 6.6, 8.1 Hz), 6.78 (1H, d, J = 7.3 Hz), 6.97 (1H, ddd, J = 1.5, 7.3, 8.1 Hz), 7.16 (1H, d, J = 7.3 Hz), 7.35 (1H, dd, J = 5.1, 6.6 Hz), 7.80 (2H, d, J = 8.1 Hz), 7.80-7.89 (1H, m), 7.97 (2H, d, J = 8.1 Hz), 8.59 (1H, d, J = 4.4 Hz), 9.59 (1H, br.s), 10.30 (1H, br.s).
IR (KBr) cm-1 = 3391,3258, 1678, 1629, 1593, 1517, 1128, 767, 742.

(0320)

Example 127.

N-(2-aminophenyl)-4-(N-(N-nicotinoyl amino) acetylamino) benzamide (Table-1 = compound number 97).

Mp. 218-220 deg C (dec.).

1H NMR (270 MHz, DMSO-d6) delta ppm: 4.13 (2H, d, J = 5.9 Hz), 4.89 (2H, s), 6.59 (1H, dd, J = 7.3, 7.3 Hz), 6.77 (1H, d, J = 8.1 Hz), 6.96 (1H, dd, J = 7.3, 8.1 Hz), 7.15 (1H, d, J = 7.3 Hz), 7.55 (1H, dd, J = 5.1, 8.1 Hz), 7.73 (2H, d, J = 8.8 Hz), 7.96 (2H, d, J = 8.8 Hz), 8.25 (1H, d, J = 8.1 Hz), 8.74 (1H, d, J = 5.1 Hz), 9.07 (1H, d, J = 1.5 Hz), 9.13 (1H, t-like, J = 5.9 Hz), 9.58 (1H, s), 10.36 (1H, s).

(0321)

Example 128.

N-(2-aminophenyl)-5-(3-(pyridin-3-yl) propionamide) benzofuran-2-carboxamido (Table-3 = compound number 1).

Mp. 267-272 deg C.

1H NMR (270 MHz, DMSO-d6) delta ppm: 2.51 (2H, t, J = 7.3 Hz), 2.97 (2H, t, J = 7.3 Hz), 6.61 (1H, dd, J = 8.1, 8.8 Hz), 6.80 (1H, dd, J = 1.5, 8.1 Hz), 6.99 (1H, dd, J = 8.1, 8.8 Hz), 7.20 (1H, dd, J = 1.5, 8.1 Hz), 7.32 (1H, dd, J = 5.2, 8.1 Hz), 7.49 (1H, dd, J = 1.5, 8.8 Hz), 7.61 (1H, d, J = 8.8 Hz), 7.67 (1H, s), 7.70 (1H, m), 8.15 (1H, d, J = 1.5 Hz), 8.40 (1H, dd, J = 1.5, 5.2 Hz), 8.51 (1H, d, J = 1.5 Hz), 9.84 (1H, s), 10.1 (1H, s).

IR (KBr) cm-1 = 3333, 3272, 1666, 1583, 1561, 1458, 1314, 1247, 1143, 807, 746, 713.

(0322)

Example 129.

Synthesis of N-(2-aminophenyl)-4-(N-(2-(pyridin-3-yl) oxy propionyl) amino) benzamide (Table-4 = compound number 2).

(129-1).

Compound 0.34 g (1.2 mmol) obtained with step of Example 47 (47-2) and compound 0.34 g (1.0 mmol) obtained with step of Example 100 (100-2) were dissolved in dichloromethane (10 ml), and

furthermore triethylamine 0.5 ml (3.6 mmol) were added. This solution was cooled with ice, and dichloromethane (5 ml) solution of 2-chloro-1,3-dimethyl imidazolinium chloride 0.21 g (1.24 mmol) was added and furthermore the mixture was stirred under ice cooling for two hours. Saturated aqueous sodium bicarbonate was added and neutralisation caused, and next it was diluted with water, and it was extracted with chloroform.

(0323)

The organic layer was washed with saturated aqueous sodium chloride solution, and thereafter it was dried, and N-(2-(N-tert-butoxycarbonyl amino) phenyl)-4-(N-(2-(pyridin-3-yl) oxy propionyl) amino) benzamide 0.68 g were obtained as mixture of 1,3-dimethyl-2-imidazolinone by refining the residue obtained by elimination by distillation of the solvent by silica gel column chromatography (ethyl acetate:methanol = 10:1).

1H-NMR (270 MHz, CDCl3) delta ppm: 1.52 (9H, s), 1.70 (3H, d, J = 6.6 Hz), 4.84 (1H, q, J = 6.6 Hz), 6.89 (1H, br.s), 7.12-7.31 (6H, m), 7.68 (2H, d, J = 8.8 Hz), 7.79 (1H, d, J = 8.1 Hz), 7.96 (2H, d, J = 8.8 Hz), 8.34 (1H, d, J = 2.9, 2.9 Hz), 8.43 (1H, d, J = 1.5 Hz), 9.25 (1H, br.s).

(0324)

(129-2) .

15 % (vol / vol) trifluoroacetic acid / dichloromethane solution (10 ml) was added at room temperature into dichloromethane (5 ml) solution of compound 0.68 g obtained with step (129-1) and the mixture was stirred for 4 hours 30 minutes at room temperature. Saturated aqueous sodium bicarbonate was added and neutralisation caused, thereafter dichloromethane was eliminated by distillation. This solution was extracted with ethyl acetate. Organic layer was washed with saturated aqueous sodium chloride solution, and thereafter was dried, and methanol and diisopropyl ether were added to the residue from which the solvent was eliminated by distillation, and the precipitated sedimentation was recovered by filtration, and by drying N-(2-aminophenyl)-4-(N-(2-(pyridin-3-yl) oxy propionyl) amino) benzamide 0.22 g (2 steps, yield 58 %) were obtained as the milk-white solid.

Mp. 193-196 deg C.

1H-NMR (270 MHz, DMSO-d6) delta ppm: 1.60 (3H, d, J = 6.6 Hz), 4.88 (2H, br.s), 5.04 (1H, q, J = 6.6 Hz), 6.60 (1H, dd, J = 6.6, 7.3 Hz), 6.78 (1H, d, J = 8.1 Hz), 6.97 (1H, dd, J = 7.3, 8.1

Hz), 7.15 (1H, d, J = 7.3 Hz), 7.32-7.39 (2H, m), 7.75 (2H, d, J = 8.8 Hz), 7.96 (2H, d, J = 8.1 Hz), 8.20 (1H, dd, J = 1.5, 3.7 Hz), 8.35 (1H, d, J = 2.1 Hz), 9.59 (1H, br.s), 10.44 (1H, br.s).

(0325)
Example 130.
Synthesis of N-(2-aminophenyl)-4-((pyridin-3-yl) methoxyacetyl amino) benzamide (Table-1 = compound number 101).

(130-1) .
To THF (300 ml) suspension of sodium hydride (60 % oil suspension form) 4.4 g (110 mmol), was added dropwise at room temperature THF (20 ml) solution of 3-pyridinemethanol 10.91 g (100 mmol) and next, the mixture was stirred at room temperature for two hours. Obtained white suspension was cooled with ice, and THF (20 ml) solution of bromoacetic acid tert-butyl 19.51 g (100 mmol) was added dropwise while keeping the internal temperature at 10-12 degrees. The mixture was stirred for three hours while being warmed this suspension to room temperature, and next, it was left to stand overnight. Water and saturated aqueous sodium bicarbonate were added and thereafter were extracted with ethyl acetate. Organic layer was washed with saturated aqueous sodium chloride solution, and thereafter it was dried, and the residue obtained by elimination by distillation of the solvent was refined by silica gel column chromatography (N-hexane:ethyl acetate = 1:1 to ethyl acetate), and (pyridin-3-yl) methoxyacetic acid tert-butyl ester 7.56 g (33.8 %) were obtained as brown oily substance.

(0326)
1H NMR (270 MHz, CDCl3) delta ppm: 1.49 (9H, s), 4.03 (2H, s), 4.64 (2H, s), 7.30 (1H, dd, J = 4.9, 7.3 Hz), 7.76 (1H, d, J = 7.3 Hz), 8.56 (1H, d, J = 4.9 Hz), 8.60 (1H, s).

(130-2) .
Trifluoroacetic acid (12 ml) was added under ice cooling in compound 3.5 g (15.7 mmol) obtained with step (130-1) and thereafter the mixture was stirred at room temperature for six hours. Thereafter, part of trifluoroacetic acid was eliminated by distillation (pyridin-3-yl), and a mixture 6.5 g of methoxyacetic acid and trifluoroacetic acid was obtained. Dichloromethane (70 ml) was added to and dissolved in this, and next pyridine (25 ml) was added. Compound 4.26 g (13 mmol) of step (100-2) of Example 100 were further added. Under ice cooling, dichloromethane solution (20

ml) of 2-chloro-1,3-dimethyl imidazolinium chloride 2.37 g (14.0 mmol) was gradually added dropwise over a period of 30 minutes.

(0327)
Furthermore the mixture was stirred for five hours and next, saturated aqueous sodium bicarbonate was added and was under ice cooling stirred till effervescence stopped at room temperature. It was extracted with chloroform, and obtained organic layer was washed with saturated aqueous sodium chloride solution, and thereafter it was dried, and the residue obtained by elimination by distillation of the solvent was refined by silica gel column chromatography (ethyl acetate to ethyl acetate:methanol = 10:1), and N-(2-(N-tert-butoxycarbonyl) aminophenyl)-4-(N-(pyridin-3-yl) methoxyacetyl amino) benzamide 4.78 g (yield 62 %) were obtained as 1:1 (mol) mixture of DMI (1,3-dimethyl-2-imidazolinone).

1H NMR (270 MHz, CDCl3) delta ppm: 1.51 (9H, s), 4.15 (2H, s), 4.70 (2H, s), 6.92 (1H, br.s), 7.15-7.29 (3H, m), 7.37 (1H, dd, J = 7.3, 5.1 Hz), 7.67 (2H, d, J = 8.8 Hz), 7.71-7.79 (2H, m), 7.96 (2H, d, J = 8.8 Hz), 8.41 (1H, s), 8.62-8.66 (2H, m), 9.23 (1H, br.s).

(0328)
(130-3) .
15 % (vol / vol) trifluoroacetic acid / dichloromethane solution (55 ml) was added into dichloromethane (28 ml) solution of compound 2.39 g (4.0 mmol) step (130-2) and the mixture was stirred at room temperature for seven hours. Saturated aqueous sodium bicarbonate was added, and it was neutralised and next water was added and was stirred at room temperature. The reaction mixture was extracted with ethyl acetate-methyl ethyl ketone (2:1), ethyl acetate-THF (2:1), ethyl acetate sequentially, and total organic layer was washed with saturated aqueous sodium chloride solution, and thereafter it was dried with anhydrous sodium sulphate. Desiccant was separated by filtration, and next, the filtrate was concentrated, and methanol and diisopropyl ether were added to obtained residue, and the precipitated solid was recovered by filtration, and N-(2-aminophenyl)-4-(N-(pyridin-3-yl) methoxyacetyl amino) benzamide 1.29 g (yield 85.6 %) were obtained as the dark brown solid by drying.

(0329)

1H NMR (270 MHz, DMSO-d6) delta ppm: 4.19 (2H, s), 4.68 (2H, s), 4.90 (2H, br.s), 6.60 (1H, ddd, J = 1.5, 7.3, 8.1 Hz), 6.78 (1H, dd, J = 1.5, 8.1 Hz), 6.97 (1H, dd, J = 7.3, 7.3 Hz), 7.15 (1H, d, J = 7.3 Hz), 7.42 (1H, dd, J = 4.4, 8.1 Hz), 7.77 (2H, d, J = 8.8 Hz), 7.85 (1H, d, J = 7.3 Hz), 7.96 (2H, d, J = 8.8 Hz), 8.54 (1H, dd, J = 1.5, 5.1 Hz), 8.63 (1H, s), 9.58 (1H, s), 10.09 (1H, s).
IR (KBr) cm-1 = 3403, 3341, 3250, 1694, 1630, 1610, 1506, 1314, 1259, 1118, 764.

(0330)
Example 131.
N-(2-aminophenyl)-4-(N-(2-(pyridin-3-yl) methoxy propionyl) amino) benzamide (the first Table-4 = compound number).

(131-1) .
Sodium hydride (60 % oil form suspension) 1.24 g (31 mmol) was suspended in dried THF (90 ml) and next dried THF (10 ml) solution of 3-pyridinemethanol 3.27 g (30 mmol) was added dropwise at room temperature over a period of five minutes. Obtained white suspension was stirred at room temperature for one hour, and thereafter dried THF (10 ml) solution of 2-bromopropionic acid tert-butyl ester 6.27 g (30 mmol) was added dropwise at room temperature over a period of five minutes. The mixture was stirred at room temperature for 11 hours 30 minutes. Water was added and thereafter was extracted with ethyl acetate. Organic layer was washed with saturated aqueous sodium chloride solution, and thereafter it was dried, and the residue from which the solvent was eliminated by distillation was refined by silica gel column chromatography (N-hexane:ethyl acetate = 1:1), thereby (pyridin-3-yl) methoxyacetic acid tert-butyl ester 4.01 g (yield 56.3 %) were obtained as dark brown oily substance.

1H-NMR (270 MHz, CDCl3) delta ppm: 1.42 (3H, d, J = 7.3 Hz), 1.50 (9H, s), 3.96 (1H, q, J = 6.6 Hz), 4.47, 4.69 (2H, ABq, J = 11.0 Hz), 7.29 (1H, dd, J = 5.1, 8.1 Hz), 7.75 (1H, d, J = 8.1 Hz), 8.50 (1H, d, J = 4.4 Hz), 8.60 (1H, s).

(0331)
(131-2) .
Trifluoroacetic acid (8 ml) was added into dichloromethane (5 ml) solution of compound 1.09 g (4.59 mmol) obtained with step (131-1) and the mixture was stirred at room temperature for nine hours 30 minutes. Dichloromethane (25 ml) was added to the residue from which the solvent was

eliminated by distillation, and furthermore pyridine (3 ml) was added. Dichloromethane (8 ml) solution of 2-chloro-1,3-dimethyl imidazolinium chloride 0.70 g (4.1 mmol) was added under ice cooling dropwise and next, the mixture was stirred for 30 minutes. Dichloromethane (20 ml)-pyridine (10 ml) solution of compound 0.98 g (3.0 mmol) obtained with step (100-2) of Example 100 was gradually added into this solution under ice cooling dropwise over a period of 15 minutes and the mixture was stirred for eight hours while being warmed to room temperature. Saturated aqueous sodium bicarbonate was added, and thereafter it was diluted with water, and it was extracted with chloroform.

(0332)
The organic layer was washed with saturated aqueous sodium chloride solution, and thereafter it was dried, and the residue which the solvent was eliminated by distillation, was refined by silica gel column chromatography (ethyl acetate-methanol = 8:1), thereby N-(2-(N-tert-butoxycarbonyl amino) phenyl)-4-(N-(2-(pyridin-3-yl) methoxy propionyl) amino) benzamide 1.19 g were obtained as 2:3 (molar ratio) mixture of 1,3-dimethyl-2-imidazolinone.

1H-NMR (270 MHz, CDCl3) delta ppm: 1.51 (9H, s), 1.54 (3H, d, J = 6.6 Hz), 4.13 (1H, q, J = 6.6 Hz), 4.65, 4.71 (2H, ABq, J = 11.7 Hz), 7.12-7.18 (2H, m), 7.28-7.37 (3H, m), 7.65 (2H, d, J = 8.1 Hz), 7.73 (2H, br.d, J = 5.9 Hz), 7.96 (2H, d, J = 8.8 Hz), 8.59-8.64 (3H, m), 9.39 (1H, br.s).

(0333)
(131-3) .
15 % (vol / vol) trifluoroacetic acid / dichloromethane solution (20 ml) was added to dichloromethane (10 ml) solution of compound 1.19 g (1.8 mmol) obtained with step (131-2) and the mixture was stirred at room temperature for four hours 30 minutes. It was poured into saturated aqueous sodium bicarbonate, thereafter aqueous layer obtained by concentrating dichloromethane was extracted with ethyl acetate. Organic layer was washed with saturated aqueous sodium chloride solution, and thereafter it was dried, and methanol and diisopropyl ether were added to the residue obtained by elimination by distillation of the solvent, and the precipitated solid was recovered by filtration, and N-(2-aminophenyl)-4-(N-(2-(pyridin-3-yl) methoxy propionyl) amino) benzamide 585 mg were obtained as the pale-brown solid by drying.

(0334)

Mp. 144-148 deg C.

1H NMR (270 MHz, DMSO-d6) delta ppm: 1.40 (3H, d, J = 6.6 Hz), 4.14 (1H, q, J = 6.6 Hz), 4.56 and 4.65 (2H, ABq, J = 11.8 Hz), 4.89 (2H, br.s), 6.60 (1H, dd, J = 7.3, 7.3 Hz), 6.78 (1H, d, J = 8.1 Hz), 6.97 (1H, dd, J = 6.6, 7.3 Hz), 7.16 (1H, d, J = 7.3 Hz), 7.40 (1H, dd, J = 4.4 Hz, 7.3 Hz), 7.78-7.85 (3H, m), 7.97 (2H, d, J = 8.8 Hz), 8.52 (1H, dd, J = 1.5, 5.1 Hz), 8.61 (1H, d, J = 2.1 Hz), 9.60 (1H, s), 10.15 (1H, s).

(0335)

Example 132.

Synthesis of N-(2-aminophenyl)-4-(N-benzylamino) carbonyl benzamide (the eighth Table-1 = compound number).

(132-1) .

Thionyl chloride (10 ml) was added dropwise to toluene (100 ml) suspension of terephthalic acid monomethyl 13.0 g (72.2 mmol) at room temperature. The mixture was stirred at 80 degrees for three hours, and next, the solvent and excess thionyl chloride was eliminated by distillation. Obtained residue was suspended in dioxane (100 ml) and next 2-nitroaniline 9.98 g (72.2 mmol) were added and it was heated under reflux for four hours.

(0336)

After cooling, thereafter the solvent was eliminated by distillation, and the obtained residue was washed with methanol, thereby N-(2-nitrophenyl)-4-methoxycarbonyl benzamide 20.3 g (yield 93.7 %) were obtained as the yellow solid.

1H NMR (270 MHz, DMSO-d6) delta ppm: 3.91 (3H, s), 7.43-7.49 (1H, m), 7.76-7.78 (2H, m), 8.03 (1H, d, J = 8.1 Hz), 8.08 (2H, d, J = 8.8 Hz), 8.14 (2H, d, J = 8.8 Hz), 10.94 (1H, s).

(0337)

(132-2) .

In THF (50 ml)-methanol (50 ml) mixed solution of compound 4.24 g (14.12 mmol) of step (132-1), was added 10 % Pd / C 0.4 g under a stream of nitrogen and thereafter the mixture was stirred under a stream of hydrogen for one hour 30 minutes. Catalyst was filtered, and the solvent was

eliminated by distillation, and the obtained residue was washed with methanol thereby N-(2-aminophenyl)-4-methoxycarbonyl benzamide 3.4 g (yield 87.5 %) were obtained as the straw-coloured solid.

1H NMR (270 MHz, DMSO-d6) delta ppm: 3.90 (3H, s), 4.95 (2H, s), 6.60 (1H, dd, J = 7.3, 8.1 Hz), 6.78 (1H, d, J = 7.3 Hz), 6.99 (1H, dd, J = 7.3, 7.3 Hz), 7.17 (1H, d, J = 7.3 Hz), 8.08 (2H, d, J = 8.1 Hz), 8.11 (2H, d, J = 8.1 Hz), 9.85 (1H, s).

(0338)
(132-3).
5 % sodium hydroxide aqueous solution was added under ice cooling into dioxane (100 ml)-water (50 ml) solution of compound 2.71 g (10.0 mmol) of step (132-2), and thereafter furthermore dioxane (40 ml) solution of di-tert-butyl di carbonate 2.62 g (12.0 mmol) was added dropwise. The mixture was stirred at room temperature for four hours, thereafter left to stand overnight. Saturated aqueous sodium chloride solution and ethyl acetate were added and were separated in bilayer, and next, aqueous layer was extracted with ethyl acetate. Organic layer was washed with saturated aqueous sodium chloride solution washed, and next, it was dried, and N-(2-(N-tert-butoxycarbonyl) aminophenyl)-4-methoxycarbonyl benzamide 3.54 g (yield 95.7 %) were obtained as the pale-brown solid by washing the residue obtained by elimination of the solvent by distillation with methanol.

1H NMR (270 MHz, DMSO-d6) delta ppm: 1.44 (9H, s), 3.90 (3H, s), 7.12-7.24 (2H, m), 7.55-7.58 (2H, m), 8.09 (2H, d, J = 8.8 Hz), 8.10 (2H, d, J = 8.8 Hz), 8.72 (1H, s), 10.00 (1H, s).

(0339)
(132-4).
Methanol (50 ml)-0. 5 N lithium hydroxide aqueous solution (25 ml) suspension of compound 3.00 g (8.10 mmol) obtained with step (132-3) was warmed at 40 degrees for five hours with stirring. Methanol was eliminated by distillation, and next, 1 N hydrochloric acid aqueous solution was added to obtained residue, and furthermore it was extracted with ethyl acetate. Organic layer was washed with little water and saturated aqueous sodium chloride solution and next, was dried. By washing the residue obtained by elimination of the solvent by distillation with methanol,

terephthalic acid mono-2-(N-tert-butoxycarbonyl) amino anilide 2.24 g (yield 77.6 %) were obtained as the pale-brown solid.

1H NMR (270 MHz, DMSO-d6) delta ppm: 1.45 (9H, s), 7.12-7.21 (2H, m), 7.53-7.58 (2H, m), 8.06 (2H, d, J = 8.8 Hz), 8.10 (2H, d, J = 8.8 Hz), 8.71 (1H, s), 9.97 (1H, s).

(0340)
(132-5) .
Benzylamine 0.14 g (1.3 mmol) were added to dichloromethane (4 ml) suspension of compound 0.20 g (0.56 mmol) obtained with step (132-4), and furthermore triethylamine 0.21 ml (1.5 mmol) were added. 2-chloro-1,3-dimethyl imidazolium chloride 0.25 g (1.48 mmol) were added under ice cooling to this solution, and furthermore the mixture was stirred under ice cooling for one hour, and the mixture was stirred for one hour at room temperature. It was diluted with chloroform, and next, water was added, and aqueous layer was extracted with chloroform.

(0341)
Saturated aqueous sodium chloride solution washed the organic layer, and next it was dried, and the residue obtained by elimination of the solvent by distillation was refined by silica gel column chromatography (chloroform:methanol = 10:1), and obtained solid was washed with ethyl ether, thereby N-(2-tert-butoxycarbonyl aminophenyl)-4-(N-benzylamino) carbonyl benzamide 279 mg (yield 62.6 %) were obtained as white solid.

1H NMR (270 MHz, DMSO-d6) delta ppm: 1.45 (9H, s), 4.52 (2H, d, J = 5.8 Hz), 7.13-7.28 (4H, m), 7.34-7.35 (3H, m), 7.56 (2H, d, J = 8.1 Hz), 8.05 (4H, s), 8.71 (1H, br.s), 9.23 (1H, t), 9.94 (1H, s).

(0342)
(132-6) .
4 N hydrochloric acid-dioxane solution (5 ml) was added at room temperature in compound 151 mg (0.339 mmol) obtained with step (132-5) and the mixture was stirred for four hours. The solvent was eliminated by distillation, and next, it was separated with ethyl acetate / saturated aqueous sodium bicarbonate, and furthermore aqueous layer was extracted with ethyl acetate to the back except precipitated sedimentation. Organic layer was washed with saturated aqueous sodium

chloride solution, and thereafter it was dried, and ethyl ether was added in the residue obtained by elimination of the solvent by distillation, and precipitated sedimentation was recovered by filtration, and N-(2-aminophenyl)-4-(N-benzylamino) carbonyl benzamide 78 mg (yield 67 %) were obtained as white solid by drying.

Mp. 239-241 deg C (dec.).
1H NMR (270 MHz, DMSO-d6) delta ppm: 4.51 (2H, s), 4.93 (2H, br.d), 6.60 (1H, dd, J = 7.3, 7.3 Hz), 6.78 (1H, d, J = 8.1 Hz), 6.95 (1H, dd, J = 7.3, 8.3 Hz), 7.18 (1H, d), 7.23-7.35 (5H, m), 8.01 (2H, d, J = 8.8 Hz), 8.07 (2H, d, J = 8.8 Hz), 9.22 (1H, br.t), 9.81 (1H, br.s).

(0343)
By process same as in Example 132, the compound of Example 133 was synthesised. Below melting point (mp.) of the compound, 1H NMR, measured value of IR are shown.

(0344)
Example 133.
N-(2-aminophenyl)-4-(N-(2-phenylethyl) amino) carbonyl benzamide (Table-1 = compound number 9).

Mp. 237-240 deg C (dec.).
1H NMR (270 MHz, DMSO-d6) delta ppm: 2.87 (2H, t, J = 7.3 Hz), 3.51 (2H, dt, J = 5.9, 7.3 Hz), 4.94 (2H, br.s), 6.60 (1H, dd, J = 7.3, 7.3 Hz), 6.78 (1H, d, J = 7.3 Hz), 6.98 (1H, dd, J = 7.3, 7.3 Hz), 7.15-7.34 (6H, m), 7.93 (2H, d, J = 8.1 Hz), 8.04 (2H, d, J = 8.1 Hz), 8.73 (1H, t, J = 5.1 Hz), 9.76 (1H, br.s).
IR (KBr) cm-1 = 3396, 3320, 1625, 1602, 1539, 1458, 1313, 699.

(0345)
Example 134.
Synthesis of N-(2-aminophenyl)-4-(N-(4-nitrophenoxy acetyl) amino) benzamide (Table-1 = compound number 54).
(134-1) .
DMF solution (5 ml) of dicyclohexylcarbodiimide 2.82 g (13.8 mmol), catalytic quantity of N,N-dimethylaminopyridine were added into DMF solution (7 ml) of 4-nitrophenoxy acetic acid 2.16 g

(11.0 mmol) and compound 3 g (9.2 mmol) of step (100-2) of Example 100, the mixture was stirred for one day. On completion of the reaction, ethyl acetate was added, and the insolubles were filtered with celite, and the solvent was eliminated by distillation.

(0346)
Obtained residue was recrystallised from chloroform, and N-(2-(tert-butoxycarbonyl amino) phenyl)-4-((4-nitrophenoxy acetyl) amino) benzamide 2.34 g (yield 50 %) were obtained.

1H NMR (270 MHz, DMSO-d6) delta ppm: 1.45 (9H, s), 4.97 (2H, s), 7.12-7.26 (3H, m), 7.23 (2H, d, J = 8.8 Hz), 7.53 (1H, dt, J = 2.2, 7.3 Hz), 7.79 (2H, d, J = 8.8 Hz), 7.95 (2H, d, J = 8.8 Hz), 8.25 (2H, d, J = 8.8 Hz), 8.71 (1H, s), 9.79 (1H, s), 10.52 (1H, s).

(0347)
(134-2) .
Iodotrimethylsilane 1.26 ml (8.85 mmol) were added at room temperature to acetonitrile solution (10 ml) of compound 0.7 g (1.38 mmol) of step (134-1), the mixture was stirred for two hours. On completion of the reaction, the solvent was concentrated and ethyl acetate was added and was stirred for 20 minutes, and the precipitated crystals were recovered by filtration. The obtained crystals were dissolved in methyl ethyl ketone, and it was washed successively with saturated sodium thiosulphate aqueous solution, saturated aqueous sodium chloride solution and was dried with anhydrous magnesium sulphate, and the solvent was eliminated by distillation. Obtained residue was washed with ethyl acetate, and N-(2-aminophenyl)-4-(N-(4-nitrophenoxy acetyl) amino) benzamide 0.22 g (yield 39 %) were obtained as the white crystals.

(0348)
Mp. 212-215 deg C (dec.) ,1H NMR (270 MHz, DMSO-d6) delta ppm: 4.97 (2H, s), 6.88 (1H, t, J = 7.3 Hz), 6.99 (1H, d, J = 7.3 Hz), 7.11 (1H, t, J = 7.3 Hz), 7.23 (2H, d, J = 8.8 Hz), 7.24 (1H, m), 7.77 (2H, d, J = 8.8 Hz), 8.00 (2H, d, J = 8.8 Hz), 8.25 (2H, d, J = 8.8 Hz), 9.89 (1H, s), 10.52 (1H, s).
IR (KBr) cm-1 = 3382, 3109, 1650, 1591, 1508, 1341.

(0349)
Example 135.

with ethyl acetate, and the organic layer was dried with magnesium sulphate, thereafter the solvent was eliminated by distillation. The obtained residue was recrystallised from ether, and N-(4-(tert-butoxycarbonyl) phenyl)-5-phenoxymethyl-1,3-oxazolidinyl-2-one 0.31 g (yield 39 %) were obtained.

1H NMR (270 MHz, DMSO-d6) delta ppm: 1.53 (9H, s), 3.97 (1H, dd, J = 6.0, 8.8 Hz), 4.23-4.34 (3H, m), 5.11 (1H, m), 6.94-7.00 (3H, m), 7.31 (2H, m), 7.71 (2H, d, J = 8.8 Hz), 7.93 (2H, d, J = 8.8 Hz).

(0352)
(136-2) .
Trimethylsilyl iodide 0.15 ml (1.05 mmol) were added to acetonitrile solution (4 ml) of compound 0.26 g of step (136-1) (0.704 mmol) and the mixture was stirred at room temperature for two hours. On completion of the reaction, the solvent was concentrated, and sludging of the obtained concentrate was carried out with ethyl acetate-methyl ethyl ketone, and N-(4-carboxy phenyl)-5-phenoxymethyl-1,3-oxazolidinyl-2-one 0.2 g (yield 91 %) were obtained.

1H NMR (270 MHz, DMSO-d6) delta ppm: 3.98 (1H, dd, J = 6.6, 9.6 Hz), 4.23-4.34 (3H, m), 5.10 (1H, m), 6.94-6.99 (3H, m), 7.30 (2H, t, J = 8.1 Hz), 7.72 (2H, d, J = 8.8 Hz), 7.98 (2H, d, J = 8.8 Hz), 12.85 (1H, s).

(0353)
(136-3) .
Catalytic quantity of DMF was added into methylene chloride solution (7 ml) of compound 0.15 g (0.479 mmol) of step (136-2) and thereafter oxalyl chloride 0.12 ml (1.40 mmol) were added and the mixture was stirred at room temperature for two hours. Thereafter the solvent was concentrated, and it was dissolved methylene chloride (4 ml) after having formed into an azeotrope twice with toluene, and methylene chloride solution (1 ml) of pyridine 0.12 g (1.52 mmol) and compound 0.105 g (0.504 mmol) of Step (1-2) of Example 1, were added under ice cooling and thereafter it was warmed to room temperature and was stirred for one hour. On completion of the reaction, water was added, and it was extracted twice with chloroform, and organic layer was washed with saturated aqueous sodium chloride solution. It was dried with magnesium sulphate, and next the solvent was eliminated by distillation. The sludging of the

Synthesis of N-(2-aminophenyl)-4-((4-aminophenoxy acetyl) amino) benzamide (Table-1 = compound number 55).

10 % Pd-C was added into methanol (15 ml)-THF (25 ml) solution of compound 1.41 g (2.78 mmol) of step (134-1) of Example 134 and the mixture was stirred at room temperature under hydrogen atmosphere for one hour. On completion of the reaction, catalyst was filtered, and the solvent was concentrated, and sludging with diisopropyl ether was carried out, and N-(2-(tert-butoxycarbonyl amino) phenyl)-4-((4-aminophenoxy acetyl) amino) benzamide 1.1 g were obtained.

(0350)
This was dissolved in acetonitrile 15 ml, and iodotrimethylsilane 0.74 ml (5.20 mmol) were added and the mixture was stirred at room temperature for three hours. On completion of the reaction, the solvent was concentrated and it was washed with methyl ethyl ketone, and N-(2-aminophenyl)-4-((4-aminophenoxy acetyl) amino) benzamide 0.86 g (yield 83 %) were obtained.

Mp. (amorphous).
1H NMR (270 MHz, DMSO-d6) delta ppm: 4.82 (2H, s), 7.13 (2H, d, J = 8.8 Hz), 7.30-7.48 (6H, m), 7.82 (2H, d, J = 8.8 Hz), 8.03 (2H, d, J = 8.8 Hz), 10.34 (1H, s), 10.46 (1H, s).
IR (KBr) cm-1 = 2873, 2590, 1680, 1602, 1505, 1243.

(0351)
Example 136.
Synthesis of N-(2-aminophenyl)-4-(5-phenoxymethyl-1,3-oxazolin-2-on-3-yl) benzamide (Table-2 = compound number 1)

(136-1)
N-butyllithium 1.33 ml (2.25 mmol) were added dropwise to THF solution (10 ml) of 4-(N-benzyloxycarbonylamino) benzoic acid t-butyl ester 0.7 g (2.14 mmol) at -78 degrees over a period of five minutes. Furthermore the mixture was stirred at the same temperature for one hour 30 minutes and next phenyl glycidol 0.31 ml (2.29 mmol) were added and further the mixture was stirred at the same temperature for one hour. It was left to stand at room temperature for one day, and next, saturated ammonium chloride aqueous solution was added, and it was extracted twice

obtained residue was carried out with isopropyl ether, and N-(2-[N-tert-butoxycarbonyl amino] phenyl)-4-(5-phenoxymethyl-1,3-oxazolin-2-on-3-yl) benzamide 0.25 g (quantitative) were obtained.

1H NMR (270 MHz, DMSO-d6) delta ppm: 1.52 (9H, s), 4.11 (1H, dd, J = 5.9, 6.6 Hz), 4.21-4.27 (3H, m), 5.01 (1H, m), 6.84 (1H, br.s), 6.91 (2H, d, J = 8.8 Hz), 7.01 (1H, t, J = 7.4 Hz), 7.12-7.34 (5H, m), 7.68 (2H, d, J = 8.8 Hz).

(0354)
(136-4) .
Trimethylsilyl iodide 0.1 ml (0.703 mmol) were added at room temperature to acetonitrile solution (4 ml) of compound 0.22 g (0.437 mmol) of step (136-3) and the mixture was stirred for two hours. Saturated sodium thiosulphate aqueous solution was added, and thereafter it was extracted twice with ethyl acetate, and organic layer was dried with magnesium sulphate, and next the solvent was eliminated by distillation. Obtained residue was recrystallised from methanol, and N-(2-aminophenyl)-4-(5-phenoxymethyl-1,3-oxazolin-2-on-3-yl) benzamide 0.13 g (yield 74 %) were obtained as the white crystals.

Mp. 165-170 deg C (dec.) .
1H NMR (270 MHz, DMSO-d6) delta ppm: 4.01 (1H, dd, J = 6.6, 9.6 Hz), 4.28-4.34 (3H, m), 5.12 (1H, m), 5.23 (2H, br.s), 6.64 (1H, t, J = 7.4 Hz), 6.81 (1H, d, J = 8.1 Hz), 6.95-7.00 (3H, m), 7.18 (1H, d, J = 6.6 Hz), 7.31 (2H, t, J = 8.1 Hz), 7.72 (2H, d, J = 8.8 Hz), 8.05 (2H, d, J = 8.8 Hz), 9.69 (1H, s).
IR (KBr) cm-1 = 3393, 1740, 1610, 1508, 1253.

(0355)
By process same as in Example 136, the compounds of Example 137 to 143 were synthesised. Below melting point (mp.) of the compound of the compound, 1H NMR, measured value of IR are shown.

(0356)
Example 137.

N-(2-aminophenyl)-4-(5-(4-nitrophenoxy) methyl-1,3-oxazolin-2-on-3-yl) benzamide (Table-2 = compound number 2).

Mp. 162-164 deg C.
1H NMR (270 MHz, DMSO-d6) delta ppm: 3.97 (1H, dd, J = 6.6, 9.5 Hz), 4.10 (1H, dd, J = 5.1, 11.0 Hz), 4.17 (1H, dd, J = 3.7, 11.0 Hz), 4.27 (1H, t, J = 8.8 Hz), 6.53-6.80 (6H, m), 6.97 (1H, t, J = 8.1 Hz), 7.16 (1H, d, J = 6.6 Hz), 7.72 (2H, d, J = 8.8 Hz), 8.04 (2H, d, J = 8.8 Hz), 9.65 (1H, s).
IR (KBr) cm-1 = 3356, 2365, 1741, 1609, 1510, 1247.

(0357)
Example 138.
N-(2-aminophenyl)-4-(5-benzyloxymethyl-1,3-oxazolin-2-on-3-yl) benzamide hydrochloride (Table-2 = hydrochloride of compound number 3).

Mp. 181-183 deg C.
1H NMR (270 MHz, DMSO-d6) delta ppm: 3.69 (1H, dd, J = 5.2, 11.0 Hz), 3.76 (1H, dd, J = 3.7, 11.0 Hz), 3.91 (1H, dd, J = 5.9, 8.8 Hz), 4.59 (2H, s), 4.93 (1H, m), 7.26-7.41 (8H, m), 7.51 (1H, m), 7.74 (2H, d, J = 8.8 Hz), 8.15 (2H, d, J = 8.8 Hz), 10.42 (1H, s).

(0358)
Example 139.
N-(2-aminophenyl)-4-(5-(pyridin-3-yl) oxymethyl-1,3-oxazolin-2-on-3-yl) benzamide (Table-2 = compound number 4).

Mp. 199-201 deg C.
1H NMR (270 MHz, DMSO-d6) delta ppm: 4.01 (1H, dd, J = 6.6, 8.8 Hz), 4.28-4.46 (3H, m), 4.96 (2H, br.s), 5.14 (1H, m), 6.61 (1H, t, J = 7.4 Hz), 6.79 (1H, d, J = 7.4 Hz), 6.98 (1H, t, J = 7.4 Hz), 7.16 (1H, d, J = 7.4 Hz), 7.36 (1H, dd, J = 4.4, 8.1 Hz), 7.44 (1H, dd, J = 1.5, 8.1 Hz).
IR (KBr) cm-1 = 2815, 2631, 2365, 1752, 1610, 1520, 1225.

(0359)
Example 140.

N-(2-aminophenyl)-4-(5-(pyridin-3-yl) methyl oxymethyl-1,3-oxazolin-2-on-3-yl) benzamide (Table-2 = compound number 5).

Mp. 160-164 deg C (dec.).
1H NMR (270 MHz, DMSO-d6) delta ppm: 3.73 (1H, dd, J = 5.2, 11.7 Hz), 3.79 (1H, dd, J = 2.9, 11.7 Hz), 3.91 (1H, dd, J = 5.9, 8.8 Hz), 4.21 (1H, t, J = 8.8 Hz), 4.62 (2H, s), 4.91 (3H, br.s), 6.60 (1H, t, J = 7.4 Hz), 6.78 (1H, d, J = 7.4 Hz), 6.98 (1H, t, J = 7.4 Hz), 7.16 (1H, d, J = 7.4 Hz), 7.38 (1H, dd, J = 4.4, 7.4 Hz), 7.69 (2H, d, J = 8.8 Hz), 7.71 (1H, m), 8.03 (2H, d, J = 8.8 Hz), 8.51 (1H, dd, J = 1.5, 4.4 Hz), 8.54 (1H, d, J = 1.5 Hz), 9.65 (1H, s).
IR (KBr) cm-1 = 3368, 1742, 1648, 1608, 1492, 1226.

(0360)
Example 141.
N-(2-aminophenyl)-4-(5-(3-nitrophenoxy) methyl-1,3-oxazolin-2-on-3-yl) benzamide (Table-2 = compound number 6).

Mp. 230 deg C (dec.).
1H NMR (270 MHz, DMSO-d6) delta ppm: 4.04 (1H, t, J = 8.8 Hz), 4.32 (1H, t, J = 8.8 Hz), 4.41-4.53 (2H, m), 4.91 (2H, s), 5.15 (1H, m), 6.61 (1H, t, J = 7.4 Hz), 6.79 (1H, d, J = 7.4 Hz), 6.98 (1H, t, J = 7.4 Hz), 7.16 (1H, d, J = 7.4 Hz), 7.46 (1H, dd, J = 1.5, 8.1 Hz), 7.61 (1H, t, J = 8.1 Hz), 7.71-7.79 (3H, m), 7.87 (1H, d, J = 8.1 Hz), 8.06 (2H, d, J = 8.8 Hz), 9.66 (1H, s).
IR (KBr) cm-1 = 3363, 3095, 2365, 1741, 1608, 1529.

(0361)
Example 142.
N-(2-aminophenyl)-4-(5-(pyridin-2-yl) methyl oxymethyl-1,3-oxazolin-2-on-3-yl) benzamide (Table-2 = compound number 7).

Mp. 172-174 deg C.
1H NMR (270 MHz, DMSO-d6) delta ppm: 3.79 (1H, dd, J = 5.2, 11.0 Hz), 3.85 (1H, dd, J = 2.9, 11.0 Hz), 3.95 (1H, dd, J = 6.6, 9.6 Hz), 4.23 (1H, t, J = 9.6 Hz), 4.67 (2H, s), 4.90 (2H, s), 4.95 (1H, m), 6.60 (1H, t, J = 7.4 Hz), 6.78 (1H, d, J = 7.4 Hz), 6.97 (1H, t, J = 7.4 Hz), 7.16 (1H, d, J

= 7.4 Hz), 7.29 (1H, dd, J = 5.2, 6.6 Hz), 7.40 (1H, d, J = 6.6 Hz), 7.70 (2H, d, J = 8.8 Hz), 7.78 (1H, dt, J = 2.2, 7.4 Hz), 8.03 (2H, d, J = 8.8 Hz), 8.51 (1H.d, J = 4.4 Hz), 9.64 (1H, s).
IR (KBr) cm-1 = 3369, 1743, 1651, 1608, 1492, 1283.

(0362)
Example 143.
N-(2-aminophenyl)-4-(5-(pyridin-2-yl) oxymethyl-1,3-oxazolin-2-on-3-yl) benzamide (Table-2 = compound number 8).

Mp. (amorphous).
1H NMR (270 MHz, DMSO-d6) delta ppm: 3.96 (1H, dd, J = 5.9, 9.6 Hz), 4.21-4.40 (3H, m), 4.90 (2H, s), 5.03 (1H, m), 6.28 (1H, t, J = 6.6 Hz), 6.43 (1H, d, J = 9.6 Hz), 6.60 (1H, t, J = 6.6 Hz), 6.78 (1H, d, J = 6.6 Hz), 6.97 (1H, t, J = 7.4 Hz), 7.15 (1H, d, J = 6.6 Hz), 7.46 (1H, dt, J = 7.4, 1.5 Hz), 7.67 (2H, d, J = 8.8 Hz), 7.69 (1H, m), 8.03 (2H, d, = 8.8 Hz), 9.64 (1H, s).

(0363)
Example 1 44.
N-(2-aminophenyl)-4-(N-(3-((pyridin-3-yl) methylamino) cyclobutene-1,2-dion-4-yl) aminomethyl) benzamide (Table-2 = compound number 9).

(144-1) .
Compound 0.1 g (0.293 mmol) of step (1-4) of Example 1 were added to THF solution (2 ml) of 3,4-di-N-butoxy-3-cyclobutene-1,2-dione 0.073 g (0.323 mmol) and the mixture was stirred for four hours and next furthermore 3-aminomethylpyridine 0.033 ml (0.327 mmol) were added and it was reacted for one day. On completion of the reaction, water was added and it was extracted twice with methyl ethyl ketone. Organic layer was dried with anhydrous magnesium sulphate, and next the solvent was eliminated by distillation.

(0364)
The sludging of the obtained residue was carried out with methanol, and N-(2-(N-tert-butoxycarbonyl amino) phenyl)-4-(N-(3-((pyridin-3-yl) methylamino) cyclobutene-1,2-dion-4-yl) aminomethyl) benzamide 0.12 g (yield 78 %) were obtained.

1H NMR (270 MHz, DMSO-d6) delta ppm: 1.44 (9H, s), 4.75-4.81 (4H, m), 7.15 (1H, dt, J = 2.2, 7.4 Hz), 7.20 (1H, dt, J = 2.2, 7.4 Hz), 7.40 (1H, dd, J = 2.2, 7.4 Hz), 7.47 (2H, d.J = 8.1 Hz), 7.54 (2H, dd, J = 2.2, 7.4 Hz), 7.73 (1H, m), 7.94 (2H, d, J = 8.1 Hz), 8.50 (1H, m), 8.55 (1H, d, J = 1.5 Hz), 8.67 (1H, s), 9.82 (1H, s).

(0365)

(144-2) .

4 N hydrochloric acid-dioxane (4 ml) was added and was reacted dioxane (4 ml)-methanol (1 ml) solution of compound 0.1 g (0.19 mmol) of step (144-1) for two hours. On completion of the reaction, the solvent was concentrated, neutralised with saturated aqueous sodium bicarbonate and thereafter methyl ethyl ketone was added r, and the obtained crystals were recovered by filtration, and N-(2-aminophenyl)-4-(N-(3-((pyridin-3-yl) methylamino) cyclobutene-1,2-dion-4-yl) aminomethyl) benzamide 0.04 g (yield 49 %) were obtained.

Mp. 230 deg C.

1H NMR (270 MHz, DMSO-d6) delta ppm: 4.76 (2H, s), 4.79 (2H, s), 4.90 (2H, s), 6.60 (1H, t, J = 7.4 Hz), 6.78 (1H, d, J = 7.4 Hz), 6.97 (1H, t, J = 7.4 Hz), 7.16 (1H, d, J = 7.4 Hz), 7.39 (1H, m), 7.43 (2H, d, J = 8.1 Hz), 7.73 (1H, d, J = 8.1 Hz), 7.97 (2H, d, J = 8.1 Hz), 7.99 (1H, br.s), 8.51 (1H, d, J = 8.1 Hz), 8.55 (1H, s), 9.64 (1H, s).

(0366)

Example 145.

N-(2-aminophenyl)-4-(3-(pyridin-3-yl) methylimidazolin-2-on-1-yl) methylbenzamide (Table-2 = compound number 10).

(145-1) .

Potassium carbonate 7.88 g (57 mmol) were added to DMF (30 ml) solution of tetra normal butylammonium iodide 1.85 g (5.0 mmol), ethylene urea 4.92 g (57 mmol), methyl 4-bromomethyl benzoate 5.73 g (25 mmol), and the mixture was heated with stirring at 80 degrees for 5 hours.

(0367)

It was allowed to cool, and thereafter solid fraction was recovered by filtration, thereafter the solid fraction was washed with ethyl acetate. The filtrate was concentrated, and next, the obtained

residue was refined by silica gel column chromatography (ethyl acetate:methanol = 10:1), diisopropyl ether was added to the obtained straw-coloured oily substance, and the precipitated solid was recovered by filtration, and N-(4-carbomethoxyphenyl methyl) imidazolin-2-one 3. 36 g (yield 57.4 %) were obtained as the pale-brown solid by drying.

1H-NMR (270 MHz, CDCl3) delta ppm: 3.28-3.35 (2H, m), 3.41-3.47 (2H, m), 3.92 (3H, s), 4.42 (2H, s), 4.61 (1H, br.s), 7.35 (2H, d, J = 8.1 Hz), 8.01 (2H, d, J = 8.1 Hz).

(0368)

(145-2) .

Saturated aqueous sodium bicarbonate was added to 3-chloromethyl pyridine hydrochloride 2.05 g (12.5 mmol) and thereafter it was extracted with ethyl acetate. Organic layer was washed with saturated aqueous sodium chloride solution, and thereafter it was dried, and toluene was added in the residue from which the solvent was eliminated by distillation, and it was formed into an azeotrope, and furthermore DMF (5 ml) was added to the obtained residue, and thereafter tetra normal butylammonium iodide 0.37 g (1.0 mmol) were added, and thereby DMF solution of benzyl halide was prepared. DMF solution (10 ml) of compound 1.17 g (5.0 mmol) obtained with step (145-1) was gradually added dropwise at room temperature to DMF (5 ml) suspension of sodium hydride (60 % oil form suspending) 0.30 g (7.5 mmol) and next, the mixture was stirred at room temperature for 30 minutes. The benzyl halide solution which was prepared beforehand was added to this solution, and thereafter it was heated with stirring at 80 degrees for 7 hours.

(0369)

It was left to stand at room temperature overnight. DMF was concentrated and next, ethyl acetate and water were added and the mixture separated. Furthermore aqueous layer was extracted with ethyl acetate-methyl ethyl ketone (2:1). The organic layer was washed with saturated aqueous sodium chloride solution, and thereafter it was dried, and the residue from which the solvent was eliminated by distillation, was refined by silica gel column chromatography (ethyl acetate:methanol = 10:1), and N-(4-carbomethoxyphenyl methyl)-N'-(pyridin-3-yl) methylimidazolin-2-one 1.17 g (yield 72.3 %) were obtained as brown oily substance.

1H NMR (270 MHz, CDCl3) delta ppm: 3.20 (4H, s), 3.92 (3H, s), 4.44 (2H, s), 4.46 (2H, s), 7.27-7.36 (3H, m), 7.64-7.69 (1H, m), 8.01 (2H, d, J = 8.1 Hz), 8.53-8.56 (2H, m).

(0370)

(145-3) .

Lithium hydroxide monohydrate 110 mg (2.62 mmol) were added at room temperature into methanol (8 ml)-water (8 ml) solution of compound 0.55 g (1.7 mmol) obtained with step (145-2), and it was heated with stirring at 50 degrees for one hour 30 minutes, and next, furthermore lithium hydroxide monohydrate 0.05 g (1.2 mmol) were added and the mixture was stirred at 50 degrees for one hour 30 minutes. It was made acidic (pH 3 or 4) using 10 % hydrochloric acid aqueous solution, and next saturated aqueous sodium chloride solution was added, and it was extracted twice with ethyl acetate and once with ethyl acetate-methyl ethyl ketones (1:1). Organic layer was dried with anhydrous sodium sulphate, and next the residue from which the solvent was eliminated by distillation was dried, thereby 4-(3-(pyridin-3-yl) methylimidazolin-2-on-1-yl) methylbenzoic acid 0.32 g (yield 61 %) were obtained as brown oily substance.

1H NMR (270 MHz, DMSO-d6) delta ppm: 3.17 (2H, s), 3.20 (2H, s), 4.36 (2H, s), 4.38 (2H, s), 7.35-7.42 (3H, m), 7.68 (1H, dd, J = 6.6 Hz), 7.92 (2H, d, J = 8.1 Hz), 8.51 (2H, m).

(0371)

(145-4) .

Oxalyl chloride 0.3 ml (3.5 mmol) were added dropwise at room temperature into dichloromethane (12 ml) solution of compound 0.31 g (1.0 mmol) obtained with step (145-3) and next, the mixture was stirred at room temperature for 30 minutes and at 40 degrees for one hour 30 minutes. The solvent was eliminated by distillation, and next it was formed into an azeotrope with toluene, and it was suspended in dichloromethane 10 ml. This reaction suspension was cooled with ice, and next, dichloromethane (2 ml)-pyridine (2 ml) solution of compound 0.21 g (1.0 mmol) of Step (1-2) of Example 1 was added dropwise. The mixture was stirred while being warmed to room temperature, and next, it was left to stand at room temperature overnight. Saturated aqueous sodium bicarbonate was added and thereafter it was extracted with chloroform.

(0372)

The organic layer was washed with saturated aqueous sodium chloride solution, and thereafter it was dried, and the residue from which the solvent was eliminated by distillation, was refined by silica gel column chromatography (ethyl acetate-methanol = 20:1), thereby N-(2-tert-

butoxycarbonyl aminophenyl)-4-(3-(pyridin-3-yl methyl) imidazolin-2-on-1-yl) methylbenzamide 0.10 g (yield 20 %) were obtained as brown oily substance.

1H NMR (270 MHz, CDCl3) delta ppm: 1.52 (9H, s), 3.20 (4H, s), 4.45 (2H, s), 4.48 (2H, s), 6.75 (1H, br.s), 7.15-7.40 (5H, m), 7.65-7.70 (2H, m), 7.83 (1H, d, J = 7.3 Hz), 7.94 (2H, d, J = 8.1 Hz), 8.50-8.60 (3H, br.m).

(0373)
(145-5) .
Compound 100 mg (0.20 mmol) obtained with step (145-4) were dissolved in dioxane (2 ml), and next, 4 N hydrochloric acid-dioxane (2 ml) was added, and thereafter methanol (0.5 ml) was added and dissolved. The mixture was stirred for two hours, and saturated aqueous sodium bicarbonate was added and neutralisation caused, and next it was extracted with ethyl acetate. Organic layer was washed with saturated aqueous sodium chloride solution, and thereafter it was dried, and the residue from which the solvent was elliminated by distillation, was dried under reduced pressure at room temperature, thereby N-(2-aminophenyl)-4-(3-(pyridin-3-yl) methylimidazolin-2-on-1-yl) methylbenzamide 47 mg (yield 58 %) were obtained as a brown oily substance.

Mp. (amorphous).
1H NMR (270 MHz, DMSO-d6) delta ppm: 3.20 (4H, s), 4.37 (2H, s), 4.39 (2H, s), 4.87 (2H, br.s), 6.60 (1H, dd, J = 7.3, 7.3 Hz), 6.78 (1H, d, J = 8.1 Hz), 6.97 (1H, dd, J = 6.6, 7.3 Hz), 7.16 (1H, d, J = 7.3 Hz), 7.35-7.41 (3H, m), 7.68 (1H, d, J = 8.1 Hz), 7.90-8.00 (2H, m), 8.50 (2H, br.s), 9.63 (1H, br.s).

(0374)
Example 146.
Synthesis of N-(2-aminophenyl)-4-(N-(pyridin-3-yl) methoxycarbonylamino methyl) benzamide 0.5 fumarate (fumarate of Table-1 = compound number 82).

Compound 310 mg obtained in Example 48 were added to methanol 10 ml, and it was heated and dissolved. Solution of fumaric acid 96 mg dissolved in methanol was added, and thereafter it was

cooled. The precipitated crystals were recovered by filtration, and it was recrystallised by methanol 5 ml, and the target substance was obtained 200 mg (yield 56 %).

(0375)

Mp. 166-167 deg C.

1H NMR (270 MHz, DMSO-d6) delta ppm: 4.28 (2H, d, J = 6.6 Hz), 5.10 (2H, s), 6.60 (1H, t, J = 8.0 Hz), 6.63 (1H, s), 6.78 (1H, d, J = 8.0 Hz), 6.90-7.50 (5H, m), 7.70-8.00 (4H, m), 8.53 (1H, d, J = 3.6 Hz), 8.60 (1H, s), 9.63 (1H, s).

IR (KBr) cm-1 = 3332, 1715, 1665, 1505, 1283, 1136, 1044, 983, 760, 712.

Elemental analysis: as C21H20N4O3+1/2C4H4O4

	C	H	N
Calculated:	63.59	5.10	12.90
Measured:	63.56	5.22	12.97

(0376)

By process same as in Example 146, the compounds of Example 147 to 149 were synthesised. Below melting point (mp.) of the compound, 1H NMR, measured value of IR are shown.

(0377)

Example 147.

N-(2-aminophenyl)-4-(N-(pyridin-3-yl) methoxycarbonylamino methyl) benzamide maleate (maleate of Table-1 = compound number 82).

Mp. 123-124 deg C.

1H NMR (270 MHz, DMSO-d6) delta ppm: 4.28 (2H, d, J = 6.6 Hz), 5.11 (2H, s), 6.24 (2H, s), 6.66 (1H, t, J = 8.0 Hz), 6.83 (1H, d, J = 8.0 Hz), 6.90-8.00 (9H, m), 8.56 (1H, d, J = 3.6 Hz), 8.62 (1H, s), 9.69 (1H, s).

IR (KBr) cm-1 = 3298, 1719, 1546, 1365, 1313, 1250, 1194, 1149, 1044, 993, 862, 751.

Elemental analysis: as C21H20N4O3+0.3H2O

	C	H	N
Calculated:	60.31	4.98	11.25

Measured:	60.52	5.12	11.03

(0378)

Example 148.

N-(2-aminophenyl)-4-(N-(pyridin-3-yl) methoxycarbonylamino methyl) benzamide hydrochloride (hydrochloride of Table-1 = compound number 82).

Mp. 140 (dec.) deg C.

1H NMR (270 MHz, DMSO-d6) delta ppm: 4.31 (2H, d, J = 5.8 Hz), 5.24 (2H, s), 7.10-7.60 (6H, m), 7.90-8.50 (5H, m), 8.70-8.90 (2H, m), 10.46 (1H, s).

IR (KBr) cm-1 = 2553, 1715, 1628, 1556, 1486, 1254, 1049, 778, 687.

(0379)

Example 149.

N-(2-aminophenyl)-4-(N-(pyridin-3-yl) oxy acetylamino methyl) benzamide 0.7 fumaric acid (fumarate of Table-1 = compound number 61).

By process same as in Example 146, it was synthesised from the compound of Example 46.

Mp. 154-155 deg C.

1H NMR (270 MHz, DMSO-d6) delta ppm: 4.42 (2H, d, J = 5.9 Hz), 4.69 (2H, s), 6.60 (1H, t, J = 8.0 Hz), 6.63 (0.7H, s), 6.78 (1H, d, J = 8.0 Hz), 6.90-7.50 (6H, m), 7.93 (2H, d, J = 8.0 Hz), 8.20-8.40 (2H, m), 8.82 (1H, br.s), 9.63 (1H, s).

IR (KBr) cm-1 = 3324, 1709, 1631, 1521, 1457, 1428, 1260, 1064, 806, 698.

Elemental analysis: as C21H20N4O3+0.7C4H4O4+0.7H2O

	C	H	N
Calculated:	60.79	5.19	11.91
Measured:	60.95	5.20	11.75

(0380)

Reference Example 1.

N-(3-aminophenyl)-4-(N-(pyridin-3-yl) methoxycarbonylamino methyl) benzamide.

It was synthesised by process same as in Example 48.

Mp. 156 deg C.
1H NMR (270 MHz, DMSO-d6) delta ppm: 4.27 (2H, d, J = 6.6 Hz), 5.06 (2H, s), 5.10 (2H, s), 6.20-6.40 (1H, m), 6.80-7.10 (3H, m), 7.30-7.50 (3H, m), 7.70-8.00 (4H, m), 8.53 (1H, d, J = 3.6 Hz), 8.59 (1H, s), 9.88 (1H, s).
IR (KBr) cm-1 = 3327, 3218, 1708, 1639, 1536, 1279, 1147, 1050, 859, 788.

(0381)
Reference Example 2.
N-(4-aminophenyl)-4-(N-(pyridin-3-yl) methoxycarbonylamino methyl) benzamide.
It was synthesised by process same as in Example 48.

Mp. 204-205 deg C.
1H NMR (270 MHz, DMSO-d6) delta ppm: 4.27 (2H, d, J = 6.6 Hz), 4.91 (2H, s), 5.10 (2H, s), 6.52 (2H, d, J = 8.8 Hz), 7.30-7.50 (5H, m), 7.70-8.00 (4H, m), 8.50-8.60 (2H, m), 9.80 (1H, s).
IR (KBr) cm-1 = 3336, 3224, 1706, 1638, 1530, 1279, 1145, 1050, 1005, 827.

(0382)
Pharmacological test example 1.
Differentiation inducing action test with respect to A 2780 cell.
Rise of alkaline phosphatase (ALP) activity is known as indicator of differentiation of human colon cancer cell, and for example sodium butyrate is known to increase ALP activity [Young et al.; Cancer Res., 45, 2976 (1985), Morita et al.; Cancer Res., 42, 4540 (1982)]. So the evaluation of differentiation induction action was carried out with ALP activity as indicator.

(0383)
(Experiment process)
A2780 cell was inoculated to 96 well plate by 0.1 ml so as to comprise 15,000 cells/well, and on the next day, solution of the test drug which was made serial dilution with culture medium was added by 0.1 ml. It was cultured for three days, and next, cells on plate were washed twice with TBS buffer (20 mM Tris, 137 mM NaCl, pH 7.6). Thereafter, p-nitrophenyl phosphate (9.6 % diethanolamine, 0.5 mM MgCl) solution of concentration of 0.6 mg/ml was added in an amount of by 0.05 ml, and it was incubated at room temperature for 30 minutes. Reaction was stopped by

3N sodium hydroxide aqueous solution 0.05 ml, and thereafter an absorbance of 405 nm was measured, and minimum concentration of drug that induced the increase of ALP activity (ALPmin) was determined.

(Experimental result)
Experimental results are shown in Table-5 (Table 31).

(0384)
(table 31)
Table-5: Differentiation inducing action with respect to A 2780 cell.

Test compound	ALPmin (μM)
Compound of Example 1	1
Compound of Example 2	3
Compound of Example 3	3
Compound of Example 4	1
Compound of Example 5	1
Compound of Example 6	1
Compound of Example 7	1
Compound of Example 8	1
Compound of Example 9	1

(0385)

Compound of Example 10	3
Compound of Example 11	1
Compound of Example 13	1
Compound of Example 15	3
Compound of Example 16	3
Compound of Example 17	3
Compound of Example 18	3
Compound of Example 23	1
Compound of Example 24	1
Compound of Example 25	3

(0386)

Compound of Example 26	1
Compound of Example 27	10
Compound of Example 28	10
Compound of Example 29	10
Compound of Example 30	0.1
Compound of Example 31	10
Compound of Example 32	3
Compound of Example 33	0.3
Compound of Example 34	0.1
Compound of Example 35	0.3

(0387)

Compound of Example 36	10
Compound of Example 37	1
Compound of Example 38	3
Compound of Example 39	0.1
Compound of Example 40	10
Compound of Example 41	0.3
Compound of Example 42	10
Compound of Example 43	3
Compound of Example 44	0.01
Compound of Example 45	0.003

(0388)

Compound of Example 46	0.1
Compound of Example 48	0.1
Compound of Example 49	1
Compound of Example 50	1
Compound of Example 51	1
Compound of Example 52	1
Compound of Example 53	3
Compound of Example 54	1

Compound of Example 55	1
Compound of Example 56	3

(0389)

Compound of Example 57	3
Compound of Example 58	3
Compound of Example 59	3
Compound of Example 60	3
Compound of Example 63	3
Compound of Example 64	3
Compound of Example 65	3
Compound of Example 66	3
Compound of Example 67	3
Compound of Example 68	3

(0390)

Compound of Example 70	0.1
Compound of Example 71	10
Compound of Example 72	10
Compound of Example 73	3
Compound of Example 74	10
Compound of Example 76	1
Compound of Example 77	3
Compound of Example 79	0.1
Compound of Example 80	0.1
Compound of Example 81	10

(0391)

Compound of Example 82	1
Compound of Example 85	3
Compound of Example 86	0.3
Compound of Example 87	0.1
Compound of Example 88	0.1

Compound of Example 89	0.3
Compound of Example 90	3
Compound of Example 91	0.1
Compound of Example 92	3
Compound of Example 93	3

(0392)

Compound of Example 94	3
Compound of Example 95	3
Compound of Example 96	10
Compound of Example 97	0.1
Compound of Example 98	0.1
Compound of Example 99	3
Compound of Example 100	1
Compound of Example 101	3
Compound of Example 102	3
Compound of Example 103	1

(0393)

Compound of Example 104	1
Compound of Example 105	1
Compound of Example 106	1
Compound of Example 107	1
Compound of Example 108	3
Compound of Example 109	1
Compound of Example 110	3
Compound of Example 111	3
Compound of Example 112	0.1
Compound of Example 113	0.3

(0394)

Compound of Example 114	3
Compound of Example 115	0.01

Compound of Example 116	0.01
Compound of Example 119	3
Compound of Example 120	0.3
Compound of Example 121	3
Compound of Example 122	0.03
Compound of Example 123	3
Compound of Example 124	3
Compound of Example 125	0.1

(0395)

Compound of Example 126	3
Compound of Example 127	0.3
Compound of Example 128	0.1
Compound of Example 129	1
Compound of Example 130	0.03
Compound of Example 131	0.3
Compound of Example 132	10
Compound of Example 133	3
Compound of Example 134	3
Compound of Example 135	3

(0396)

Compound of Example 136	1
Compound of Example 137	1
Compound of Example 138	1
Compound of Example 139	0.3
Compound of Example 140	0.3
Compound of Example 141	1
Compound of Example 142	0.1
Compound of Example 143	3
Compound of Example 145	3
Compound of Comp.Ex. 1	>;100
Compound of Comp.Ex. 2	>;100

(0397)

Pharmacological test example 2.

Antitumour test.

(experiment process) .

Mouse myelogenic leukaemia cells WEHI-3 (1-3 x 10 power 6 cells) were transplanted to Bal b/c mouse intraperitoneally, and administration of drug was started from the next day. This comprised day 1, and thereafter the drug was orally-administered once per day on day 1-4 and day 7-11. Survival time after transplantation was observed, and ratio of survival time of drug treated group with respect to survival time of Control group (T/C, %) was calculated, and this was evaluated as macrobiotic effect.

(experimental result) .

Experimental result was shown in Table-6 (Table 32).

(0398)

(Table 32)

Table-6: Antitumour action with respect to WEHI-3 cell

Test compound	dosage (μmol /k g)	T/C (%).
Compound of Example 45	16	138
Compound of Example 46	32	141
Compound of Example 48	130	190
Compound of Example 130	130	189

(0399)

Pharmacological test example 3.

Antitumour action test

(experiment process) .

Tumour cells which was subcutaneously subcultured in the nude mouse (HT-29, KB-3-1) were transplanted to nude mouse, and when the volume became around 20-100 mm power 3 and the survival was confirmed, the administration of drug was started. This comprised day 1, and the drug was orally-administered thereafter on 1-5 day, day 8-12, day 15-19 and day 22-26. Tumour volume was determined by (tumour volume) = 1/2 x (long axis length) x (short axis length) 2.

(0400)
(experimental result) .
Experimental results of the compound of Example 48 with respect to HT-29 (dosage 66 μmol/kg) are shown in Figure 1.

(0401)
Experimental results of the compound of Example 48 with respect to KB-3-1 (dosage 66 μmol/kg) are shown in Figure 2.

(0402)
Calculation Example.
(Assembly of superimposition model by highly active compounds) .
The compounds of Example 45 Example 46 and Example 48 which demonstrated high differentiation induction activity, were used, and superimposition of three dimensional structures was performed in order to extract the information on spatial arrangement of the atomic groups necessary for the expression of activity.

(0403)
For this purpose, the same analysis can be carried out using any commercial calculation packages [CATALYST (MSI company), Cerius2/QSAR+ (MSI company), SYBYL/DISCO (Tripos company)], but SYBYL/DISCO (Tripos Company) was used for the production of this superimposition structure and analysis.

(0404)
Three dimensional structure was generated using sketch function of SYBYL with respect to the compound of Example 48, and dot charge was generated on each atom by Gasteiger-Huckel method, and next, structural optimisation was performed using Tripos force field. Thereafter dummy atoms were placed on the possible interaction sites in order to identify the sites in which interactions such as hydrophobic interaction site (aromatic ring, aliphatic side chain) and hydrogen bond site (carbonyl oxygen, hydroxyl group, amino group and the like), which was thought to be important for drug-living body interaction site.

(0405)
During this, in order to distinguish interactions such as hydrophobic interaction, hydrogen bond and electrostatic interaction site, interactions were classified, and different dummy atom types for each interaction were established. Furthermore, conformers in which rotatable bonds were rotated were generated, and ones in which the distance of the dummy atoms arranged on the imagined interaction site were stored as novel conformation in conformation file. Construction of three dimensional structure and generation of conformation were performed for the compounds of Example 45 and Example 46 in the same way.

(0406)
The compound of Example 48 was used as template molecule, for each confirmation, superimposition structures were constructed so that all the dummy atoms which demonstrated the same types of interaction with respect to all conformations of the compound of Example 45 and Example 46 were superimposed.

(0407)
For the obtained superimposition structures, the optimum superimposition structure was selected based on the number of superimposed atoms (the number of common interactions), degree of three dimensional superimposition (superimposition volume) and three dimensional QSAR analysis results using activity value.

(0408)
Fro the superimposition structure obtained this time, it was indicated that the centre of gravity (W1) of B ring of the compound of formula (13), centre of gravity (W2) and hydrogen bond receptor (carbonyl oxygen and the like) (W3) of A ring assumed W1-W2 = 8.34 Å, W1-W3 = 3.80 Å, configuration of W2-W3 = 5.55 Å.

(0409)
(calculation example 1 = the compound of Example 130).
Suitable 7 atoms were selected from imagined interaction site of the compound of Example 130 and structural atom of benzamide structure, the structural optimisation was carried out by imposing constraint potential to the compound of Example 130 and using the compounds of aforesaid Example 45, Example 46 and Example 48 sued for aforesaid superimposition structure as target

structure. Next, the constraint potential was removed, and the structural optimisation was carried out, and the active conformation of the compound of Example 130 was obtained. With respect to this active conformation, the centre of gravity (W1) of benzene ring of benzamide and centre of gravity (W2) and carbonyl oxygen (W3) of pyridine ring were defined, and extraction of parameter of spatial arrangement was performed.

(0410)
Moreover, all conformations with respect to the rotatable bonds were generated, and energy for each conformation was calculated, and the most stable structure was determined. Energy of the most stable structure was calculated, and energy difference of active conformation was determined. As a result, in the structure which was obtained this time, it was indicated to have configuration of W1-W2 = 8.43 Å, W1-W3 = 3.82 Å, W2-W3 = 5.88 Å (energy difference from the most stable structure = 2.86 kcal/mol).

(0411)
Moreover, the same results were obtained by carrying out analysis procedure using dummy atoms obtained by construction of aforesaid superimposed structure.

(calculation results). Calculation results were shown in Table-7 (Table 33).

Table-7: Calculation results of parameter of spatial arrangement.

(0412)
(Table 33)

Compound	W1-W2 (Å)	W1-W3 (Å)	W2-W3 (Å)
Compound of Example 39	8.20	3.95	5.49
Compound of Example 45	8.54	3.85	5.55
Compound of Example 46	7.42	3.97	5.93
Compound of Example 47	8.52	3.88	5.69
Compound of Example 48	8.43	3.94	5.51
Compound of Example 79	7.09	5.20	5.48
Compound of Example 80	8.59	4.37	5.51
Compound of Example 87	6.80	3.80	3.63

(0413)			
Compound of Example 88	8.67	3.50	6.22
Compound of Example 124	8.29	3.75	6.42
Compound of Example 128	8.64	3.76	5.90
Compound of Example 130	8.43	3.82	5.88
Compound of Example 131	8.59	4.88	5.47
Compound of Example 136	7.59	3.94	7.27
Compound of Example 137	7.58	3.94	7.27
(0414)			
Compound of Example 138	9.07	3.94	7.47
Compound of Example 139	7.64	3.94	7.29
Compound of Example 140	9.11	3.94	7.50
Compound of Example 141	7.60	3.94	7.28
Compound of Example 124	9.02	3.94	7.44
Compound of Example 143	7.62	3.94	7.29
Compound of Example 145	8.48	4.40	5.69

(0415)

Advantages Afforded by this Invention.

Novel benzamides and novel anilide derivative of this invention have differentiation induction action and is useful as drug such as therapy • improvement drug for malignant tumour, autoimmune disease, dermatopathia, parasite infestation. In particular, the effect as carcinostatic is high and effective in hematopoietic organ tumour, solid cancer.

Brief Description of the Figures

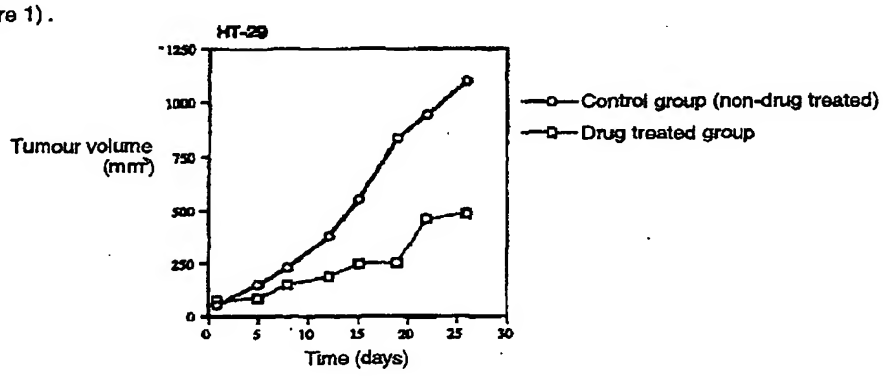
(Figure 1).

It is Figure to show change of tumour volume during the compound administration of Example 48 with respect to tumour cell (HT-29).

(Figure 2).

It is Figure to show change of tumour volume during the compound administration of Example 48 with respect to tumour cell (KB-3-1).

(Figure 1).



(Figure 2).